RADIOLOGY

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EDITOR

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Intracranial Angiography[1]

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THE RAPID and extensive development of intracranial surgery during the past twenty years has been facilitated in great measure by the employment of x-ray procedures by means of which it is possible to investigate the skull and its contents in great detail prior to direct surgical exploration. The oldest and simplest of these, *x-ray examination of the cranial bones*, depends for evidence of underlying brain lesions upon the discovery of associated osseous abnormalities. A few lesions, characteristically associated with lime salt deposition in otherwise radiolucent tissues, cast recognizable shadows in their own right. Although this form of study is useful, it is often found wanting when the need for detailed diagnostic information is greatest.

Intracranial pneumography, which consists of the graphic portrayal of anatomical landmarks in contrast to gas temporarily introduced into cerebrospinal fluid spaces, enormously broadens the usefulness of x-rays. Many lesions entirely unrecognizable by ordinary radiographic methods may be identified and described in considerable detail when pneumography is employed.

Radiographic examination of the skull following the perfusion of intracranial vessels with radiopaque materials is known as *intracranial angiography*. Blood vessels, momentarily rendered densely opaque, serve as reference points in detecting disturbances of anatomical relationships produced by intracranial lesions. This method, very useful when vascular displacement provides evidence of disease in neighboring tissues, is of special value when the vessels are involved directly. In particular, the procedure offers a means of obtaining diagnostic information not otherwise available in suspected intracranial aneurysms, anomalies of intracranial vessels, certain cases of arterial occlusion, and expanding lesions involving one cerebral hemisphere which have not been accurately localized. Sometimes the vascular pattern provides an indication of the character of the pathological process.

Angiography, as applied to the arteries and veins of the extremities, has long been accepted as a useful procedure. The principle was first applied to the circulatory system of the cerebrum in June 1927, by Egas Moniz of Lisbon (1, 2), who injected the carotid system with 70 per cent strontium bromide. Of six patients so examined, one died as a result of the procedure. Twenty-five per cent sodium iodide was then substituted for strontium bromide,

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and approximately 200 patients were injected over a period of three years. Cerebral vessel shadows proved much more satisfactory in this group, but many of the patients suffered headaches, convulsions, and transient hemiplegia. In two instances death occurred. In 1931 Egas Moniz abandoned the use of sodium iodide and began to inject patients with thorotrast, which material he has used successfully since that date.

The significance of intracranial angiography was soon recognized in other European clinics. In Germany the method was introduced by Löhr and Jacobi in 1931 (3) and later was extensively employed for the diagnosis of brain tumors by Tönnis (4), Fischer (5), and Lorenz (6). In England carotid angiography was adopted by Dott (7) and by Jefferson and Northfield (8); in Sweden by Olivecrona. Physicians of North America have been slow to follow the European lead, the first protagonists of the method being Elvidge (9) and Turnbull (10) in Canada, Freeman and Watts (11) and Gross (12) in the United States. Expansion of the angiographic procedure to include the portions of the brain whose blood supply is derived from the vertebral arteries was first described by Egas Moniz, Pinto, and Alves (13) in 1933, and technical modifications were proposed by Sjöquist (14) in 1938 and by King (15) in 1942.

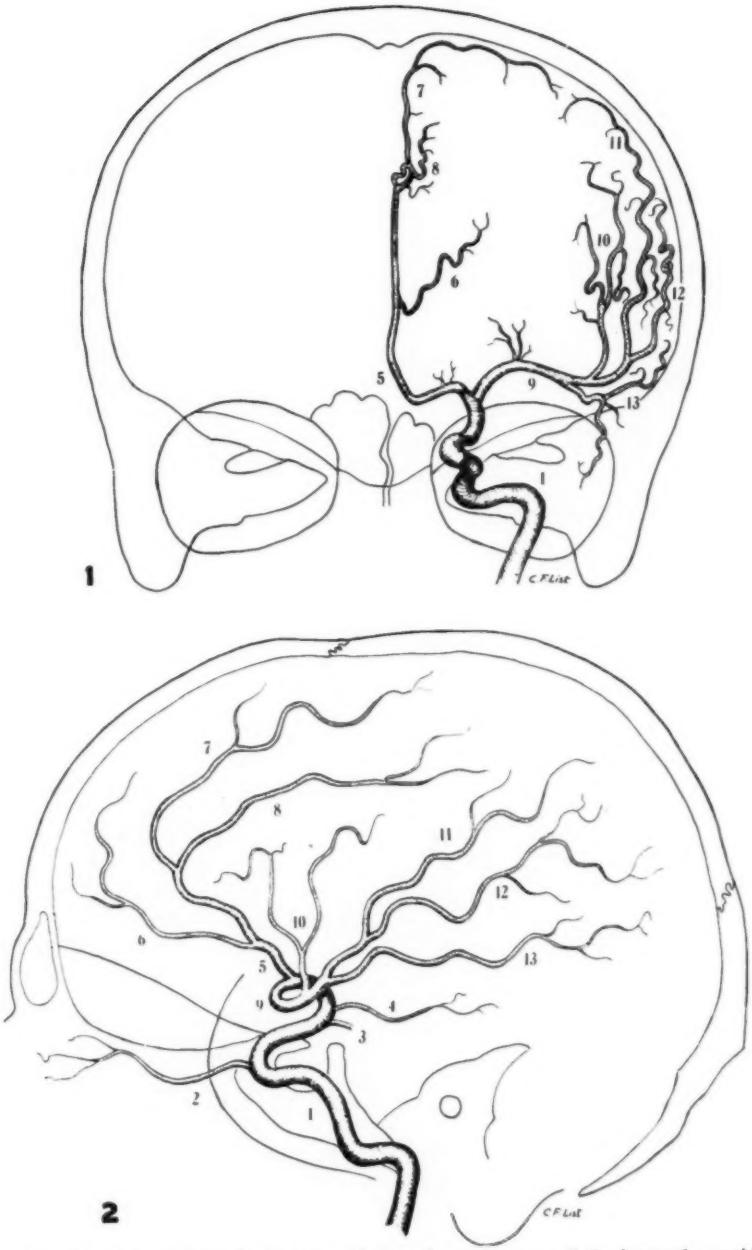
At the University Hospital (Ann Arbor) intracranial angiography has been used systematically since January 1941 in situations where this method of study appeared to offer the likelihood of solving particularly difficult diagnostic problems. In some three years, 127 patients have been subjected to this type of examination. In the bulk of these the carotid system was injected; vertebral arteriography was used in six instances only.

ANATOMICAL CONSIDERATIONS

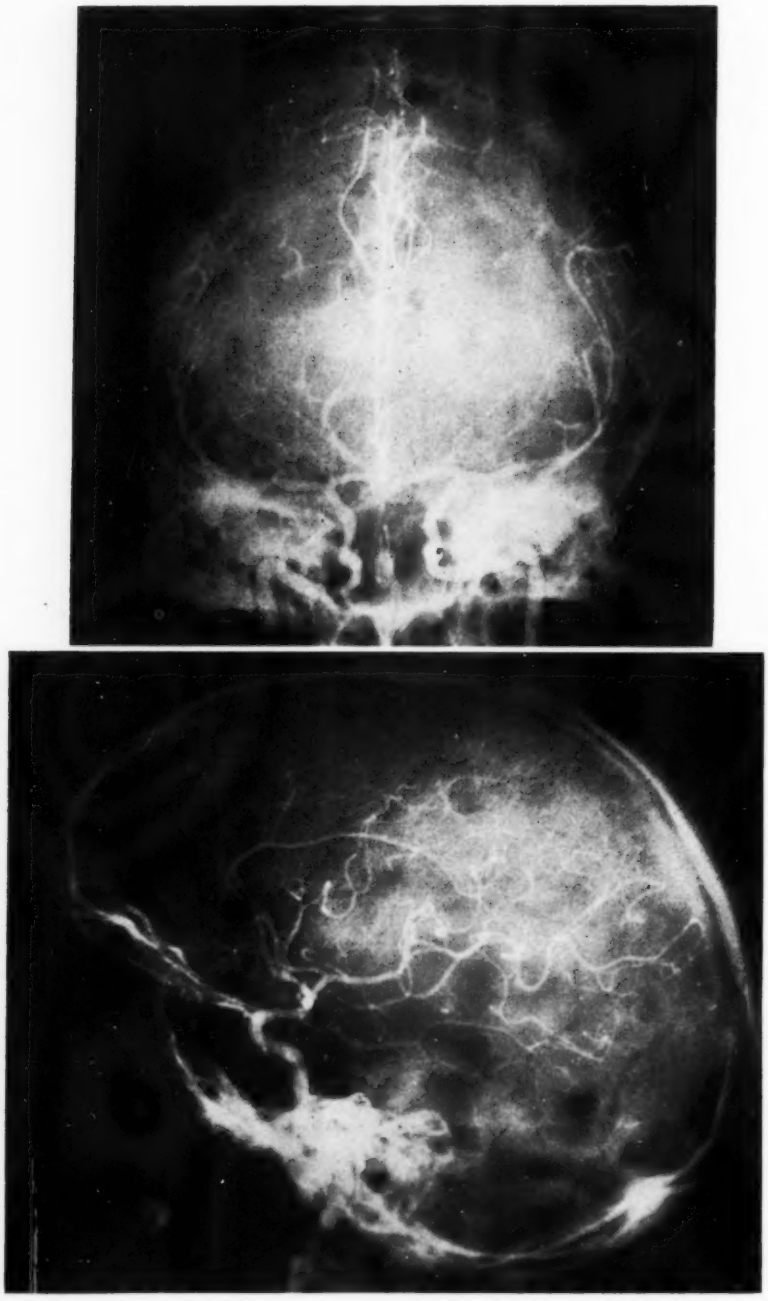
If the vessels which supply blood to the brain are to be used as a system of landmarks, by means of which lesions involving the brain substance can be identified and localized, the observer must be familiar with the intimate anatomical details of the circulatory system of the brain. When, by means of opaque perfusion, these vessels are seen for the first time in roentgenograms of the skulls of living patients, the intricacies and complexities of their arborizations are bewildering. It is necessary to use frontal and lateral projections of the skull or stereoscopic lateral projection to appreciate the fact that the major branches of the internal carotid lie close to the brain surface.

Entering the cranial vault, the internal carotid artery divides into two major divisions, the anterior and middle cerebral arteries, whose zones of distribution are strikingly characteristic. The branches of the anterior cerebral artery supply the medial surface of the hemisphere over its anterior two-thirds. The middle cerebral artery courses lateralward along the sylvian fissure to the convex surface of the cerebrum. The medial and under surfaces of the temporal and occipital lobes receive blood from the posterior cerebral artery, which arises from the vertebral system. The brain stem and the cerebellum are exclusively supplied by the vertebral arteries. It is obvious that injections of the internal carotid are useful when supratentorial structures are to be examined, whereas angiographic exploration of the posterior fossa necessitates injection of the vertebral system.

When one thinks of the carotid system in terms of sagittal, lateral, and basilar surfaces of the cerebral hemisphere, it becomes considerably easier to use angiography as a graphic method of detecting abnormalities in the brain substance which is surrounded by this vascular network (Figs. 1, 2, 3, 4). Sizable space-occupying masses may displace or distort the vessels which extend over one or all of these surfaces. Alterations of the course, location, or the caliber of particular vessels can be translated in terms of specific neurological structures to localize the causative lesion. For purposes of reference, a detailed anatomical description of the subdivisions of



Figs. 1 and 2. Schematic drawings of normal arteriograms of the internal carotid artery (1. Anteroposterior projection. 2. Lateral projection).
1. Internal carotid artery. 2. Ophthalmic artery. 3. Posterior communicating artery. 4. Anterior choroidal artery. 5. Anterior cerebral artery. 6. Frontopolar artery. 7. Callosomarginal artery. 8. Pericallosal artery. 9. Middle cerebral artery. 10. Ascending frontoparietal artery. 11. Posterior parietal artery. 12. Angular artery. 13. Posterior temporal artery.



Figs. 3 and 4. Carotid arteriograms in anteroposterior (above) and lateral (below) projections.

The bilateral anteroposterior arteriogram was obtained by simultaneous injection of both internal carotids. Except for moderate lateral displacement of the sylvian group, due to internal hydrocephalus, the picture is not grossly abnormal. Note that the anterior communicant artery, connecting both anterior cerebrals, is very short.

In the lateral view the posterior communicant and posterior cerebral arteries are plainly visible, an anatomical variation occurring in 15 per cent of all cases.

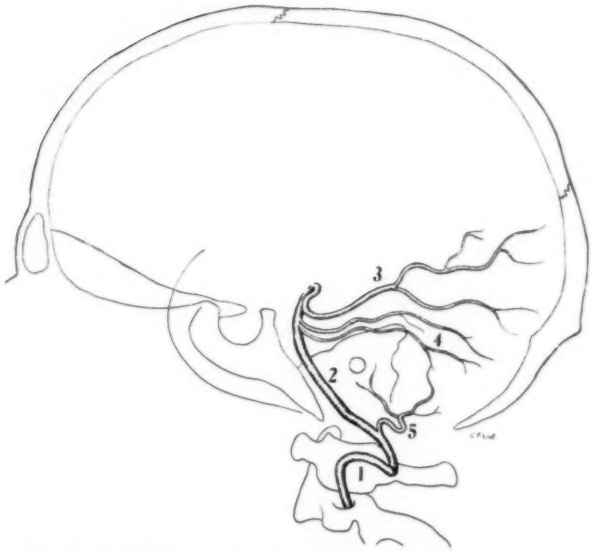


Fig. 5. Schematic drawing of a normal vertebral arteriogram in lateral projection. 1. Vertebral artery. 2. Basilar artery. 3. Posterior cerebral artery. 4. Superior cerebellar artery. 5. Posterior inferior cerebellar artery.

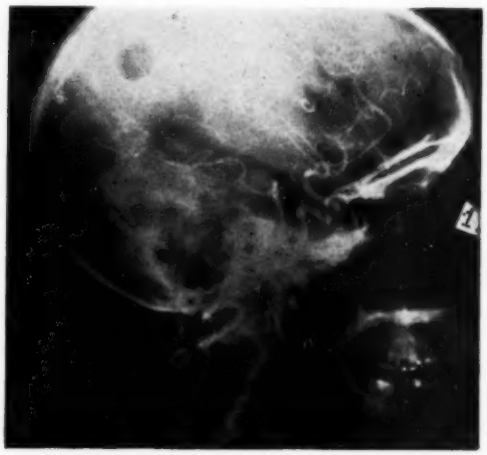


Fig. 6. Normal vertebral arteriogram in lateral projection. The picture was obtained by retrograde injection into the subclavian artery. Due to overflow, the contrast medium has also filled the carotid system. Faint gas shadows are visible from previous ventriculography.

the internal carotid, stressing relationships of practical importance in angiographic diagnosis is appended (Anatomical Notes, A).

Angiography is commonly limited to the study of supratentorial lesions because the technical procedure is somewhat simpler and because results are more satisfactory than in the case of posterior fossa lesions. It is important, however, to be prepared

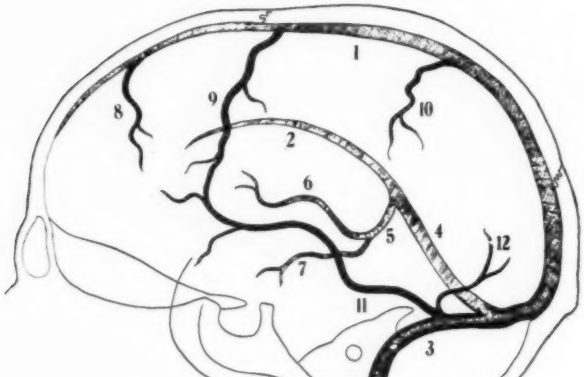


Fig. 7. Schematic drawing of normal venogram in lateral projection, obtained by carotid injection. Superficial veins are shaded more darkly than the sinuses and deep veins.
1. Superior sagittal sinus. 2. Inferior sagittal sinus. 3. Transverse sinus. 4. Straight sinus. 5. Great cerebral vein of Galen. 6. Internal cerebral vein. 7. Basal vein of Rosenthal. 8. Frontal ascending vein. 9. Rolandic vein of Trolard. 10. Parietal ascending vein. 11. Communicating temporal vein of Labbé. 12. Descending temporo-occipital vein.

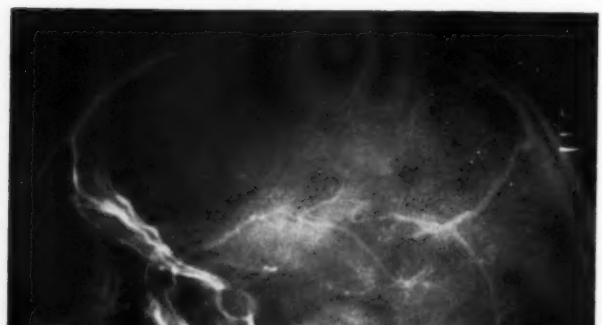


Fig. 8. Normal venogram in lateral projection obtained by carotid injection. The sinuses are only incompletely filled. A large superficial sylvian vein is visible at the anterior part of the temporal lobe.

to examine the structures beneath the tentorium and for that reason a description of the vertebral system (Figs. 5 and 6) is also appended (Anatomical Notes, B).

Opaque material, distributed by the arteries, is reaccumulated by the cerebral veins, which can be demonstrated in properly timed roentgenograms. Some

familiarity with the anatomy of the venous system is necessary if one is to employ venograms for purposes of accurate diagnosis (Figs. 7 and 8). Here again the general scheme may be described in simple terms. Venous channels within the cranial vault consist of three systems—superficial veins, deep veins, and venous sinuses. Blood from the brain surface is collected by the superficial vessels and by them transmitted to the superior sagittal and lateral sinuses. Blood from the basal ganglia is collected by the deep cerebral veins which lead to the straight sinus. A detailed description of the intracranial venous system is presented below (Anatomical Notes, C).

ANATOMICAL NOTES

A. Carotid Arteriogram

The internal carotid artery enters the skull through the carotid canal at the tip of the petrous apex. It passes through the cavernous sinus and, after penetration of the dura, terminates by bifurcation into the anterior and middle cerebral arteries. According to Egas Moniz, the curved intracranial portion of the internal carotid, also called the carotid siphon, forms a simple S-curve (31 per cent), a double S-curve (39 per cent), or a transitional form (30 per cent). The first large intracranial branch, visible in most carotid arteriograms, is the ophthalmic artery. It extends forward from the internal carotid just below the level of the anterior clinoid and enters the orbit through the optic foramen. The next direct branch, the posterior communicating artery, is seldom demonstrated, but in 15 per cent of all cases is so large that the posterior cerebral artery can be considered as arising from the internal carotid. The last branch of the internal carotid before its bifurcation is the anterior choroidal artery, a small yet fairly constant vessel. It passes backward between the medial surface of the temporal lobe and the cerebral peduncle along the optic tract to end in the glomus choroideus of the lateral ventricle.

The middle cerebral artery first courses lateralward in the sylvian fissure, giving off small branches to the basal ganglia, and then turns backward and upward on the surface of the insula, where it gives off several small vertically ascending branches, the largest of which supplies the lower frontoparietal (rolandic) area and has roughly the configuration of the Greek letter ψ. The terminal three branches of the middle cerebral artery, which course diagonally backward and upward in the sylvian fissure, are the posterior parietal artery supplying the convexity of the parietal lobe; the angular (*pli courbé*) branch supplying the angular gyrus and parieto-occipital convexity; and the posterior temporal artery supplying the posterior and superior portions of the temporal lobe. Collectively the last three branches are known as the middle cerebral or sylvian group.

The anterior cerebral artery passes forward and medialward to the longitudinal fissure. It then curves around the genu of the corpus callosum, giving off the frontopolar branch, which passes forward on the medial surface of the cerebral hemisphere toward the frontal pole. The anterior cerebral artery finally turns backward along the medial surface of the cerebral hemisphere and divides into pericallosal and callosomarginal branches, which extend posteriorly.

B. Vertebral Arteriogram

The vertebral artery winds behind the superior process of the atlas and, after entering the skull through the foramen magnum, passes upward and medially in close contact with the base of the posterior cranial fossa and ventral surface of the medulla. Its first intracranial branch is the posterior inferior cerebellar artery, which supplies the ventrolateral portion of the cerebellum and medulla. At the pontomedullary junction, the vertebral artery joins the vessel of the opposite side to form the basilar artery, which lies in the mid-line between the clivus and the pons and ends in the interpeduncular space. The basilar artery gives off small pontine branches bilaterally, among them the anterior inferior cerebellar arteries and the superior cerebellar arteries which supply the dorsal surface of the cerebellum and dorsal portion of the midbrain. The basilar artery terminates by dividing into the two posterior cerebral arteries, which are the only supratentorial branches of the vertebral system. Each posterior cerebral artery winds around the cerebral peduncle and, following the basilar surface of the temporal and occipital lobes, courses toward the occipital pole and typically divides into two large terminal branches. The posterior communicating artery is not demonstrated by vertebral arteriography, but, as mentioned before, when this vessel is large it may be shown with the posterior cerebral artery by carotid injection.

C. Venogram Obtained by Carotid Injection

Intracranial venous channels can be divided into three systems—superficial cerebral veins, deep cerebral veins, and venous sinuses. The superficial cerebral veins collect blood from the cortex and empty mainly into the superior sagittal and lateral sinuses. There is a variable number of roughly parallel frontal, parietal, and occipital cortical veins which follow the sulci of the brain to the superior sagittal sinus. One of the largest of these is the great anastomotic vein of Trolard, which is located in the posterior frontal (rolandic) area. In the region of the temporal lobe the superior sylvian vein continues into the posterior anastomotic vein of

Labbé, which passes posteriorly and inferiorly across the temporal lobe to the lateral sinus. This sinus also receives some smaller tributaries from the inferior surface of the temporal lobe.

The deep cerebral veins drain the basal ganglia. The two internal cerebral veins are located in the tela choroidea on the dorsal surface of each thalamus. They receive the basal veins of Rosenthal, which come from the base of the brain around the cerebral peduncles. The junction of the internal cerebral veins forms the great cerebral vein of Galen, which is median in position, very short, and terminates in the straight sinus.

The superior sagittal sinus is located in the superior portion of the falx cerebri and ends in the confluens sinuum by joining in the straight and lateral sinuses. The smaller inferior sagittal sinus is located in the inferior edges of the falx; it forms the straight sinus by junction with the vein of Galen. Egas Moniz has pointed out that the straight sinus is a direct continuation of the inferior sagittal sinus and that the vein of Galen joins it at an acute angle. This is contradictory to older anatomical teachings based on studies of cadavers. The posterior portion of the inferior sagittal sinus and the vein of Galen outline the splenium of the corpus callosum. The *venogram* obtained by *vertebral injection* demonstrates numerous superficial cerebellar veins. Most of them collect on the dorsal surface of the cerebellum and drain into the transverse sinus or into the straight sinus forming a vascular plexus in the pineal area.

PHYSIOLOGICAL CONSIDERATIONS

Normally it requires about four seconds for blood to pass from the carotid artery by way of the various cerebral vessels and their capillary networks to the large intracranial venous sinuses. By proper timing of injection and exposure, either the arterial or the venous phase of the cerebral circulation can be recorded without difficulty. The arterial phase lasts throughout the first second following injection. The capillary phase, recognizable in angiograms by generalized increase in soft-tissue density, is very brief, for within three seconds after injection the veins begin to fill, and lastly the venous sinuses. Blood from the vertebral arteries reaches the venous sinuses after a slightly longer period.

If stereoscopic filming is to be done, time relations must be exactly duplicated during two separate injections of opaque material. By means of dexterous teamwork perfected by frequent practice, it is possible to produce two pairs of stereoscopic films representing an arteriogram and a venogram of the same patient with but two injections of contrast material.

Increased intracranial pressure and widespread venous stasis prolong intracranial circulation time. Partial vascular occlusion, aneurysm, and certain neoplasms may produce localized slowing of blood flow. In order to obtain maximum contrast between injected blood vessels and normally translucent surrounding brain tissue, conditions which lead to excessive dilution of the opaque mass with normal blood are to be avoided. Opaque material must be injected briskly, being added to the normal inflow of blood from the carotid on the side being studied. This is necessary in order to prevent the anterior cerebral artery from being flooded from the contralateral side by way of the anterior communicating artery. When this does occur, some of the branches which one desires to observe may be filled with normal blood instead of blood which has been mixed with opaque material.

TECHNIC

Surgical Procedures

Carotid Angiography: Local anesthesia is used. Preoperative anticonvulsive medication is desirable in the case of patients who are known to have had convulsions.

The carotid bifurcation is exposed by means of a 5- to 8-cm. incision parallel to the sternomastoid muscle (Fig. 9, 1). After incision of skin, subcutaneous tissue, and platysma, and after lateral retraction of the sternomastoid muscle, the sheath of the great vessels is entered. In retracting the internal jugular vein, one or more deep facial veins are sometimes in the way and may have to be retracted or, rarely, ligated and cut. Segments of the common, internal, and external carotid arteries are dissected free and stripped of adventitia. Untoward systemic reactions resulting from the carotid sinus reflex are avoided by local injection of procaine. A thin rubber strip is placed around the common carotid,

and another around the beginning of the external carotid. The common and internal carotid arteries are elevated with pledgets of cotton. The patient is now transferred to the x-ray table. For lateral projection, the head is turned toward the unoperated side; the side to be injected is farthest from the film. Immobilization of head and shoulders is important.

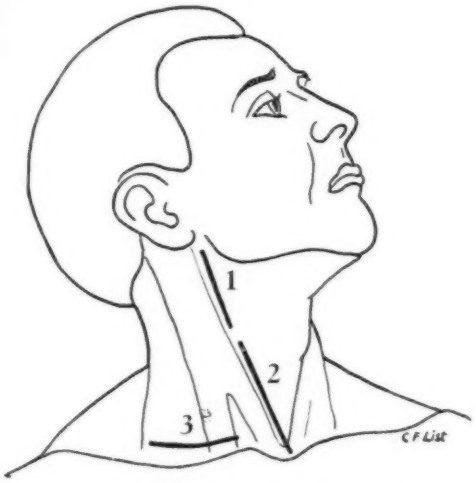


Fig. 9. Schematic drawing to show the surgical incisions used for arteriography. 1. For carotid injection. 2. For direct vertebral injection. 3. For indirect vertebral injection (retrograde subclavian injection).

Injection equipment consists of three 10-c.c. and three 20-c.c. Luer syringes, an 18- or 19-gauge needle of medium bevel, 3 to 4 cm. in length, and a 10-cm. length of pliable though non-collapsible rubber tubing fitted on either end with adaptors. Syringes, adaptors, and tubing must be well tested in advance; they must not fail when used at high speed under considerable pressure.

The common carotid is elevated, but not strangulated, by means of the rubber strip. The external carotid is pulled upward slightly and is purposely strangulated by twisting its rubber strip. The needle-tube-syringe combination is filled with the injection material. The needle puncture is made in the internal carotid at its origin or in the common carotid just proximal to the bifurcation. In the latter case, the

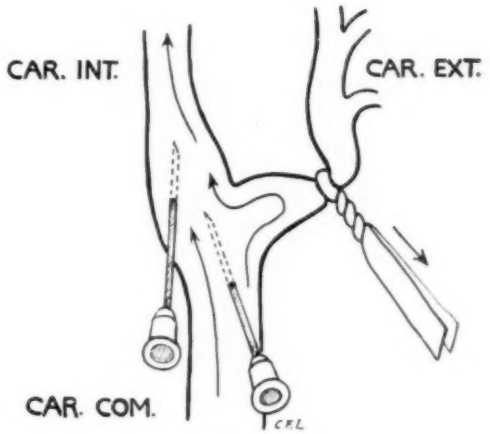


Fig. 10. Schematic drawing to show the technic of carotid arteriography. The external carotid is strangulated and the injection is made either into the internal carotid or common carotid below the bifurcation.

point of the needle is directed toward the orifice of the internal carotid (Fig. 10). If the patient's neck is short, or if the bifurcation is highly placed, injection by way of the common carotid is the method of choice. Great care is taken to avoid multiple arterial punctures. When the needle is in proper position, the arterial blood pressure will push back the plunger of the syringe and the needle will be gripped by the elasticity of the arterial wall so that it is not necessary to hold the needle firmly. Ordinarily three injections are made, two to obtain stereoscopic lateral views, and the third for a single anteroposterior projection. A total of five films are exposed. Each injection consists of 10 c.c. (8 to 12 c.c. may be used). The opaque material is forced into the artery as rapidly as possible. When the first injection is two-thirds complete, the signal is called for beginning of the x-ray exposure. As soon as the film can be changed, usually about three seconds after the injection is completed, a second exposure is made. This is intended to record venous return.

Without disturbing the needle and tubing, the empty syringe is replaced by a 20-c.c. syringe containing Ringer's solution, and the rubber tubing and needle are flushed to prevent clotting. The x-ray

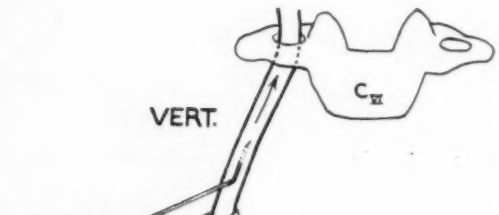


Fig. 11. Schematic drawing to show the technic of direct vertebral arteriography.

tube is then shifted for stereoscopy and a second injection is performed in an identical manner. Following the second injection, the tubing and needle are flushed continuously with Ringer's solution until the head is rotated to the anteroposterior position.

To expose the skull in this direction, the x-ray tube is angled so that its beam will pass through a plane which includes the external auditory meatus and a point in the mid-line of the forehead 5 cm. above the glabella. A third injection is made and, due to the longer exposure time used for this projection, the signal for starting the x-ray exposure is given immediately after the injection is begun. No venogram is made in this instance.

Strangulation of the external carotid is then discontinued, the needle is withdrawn, and hemostasis is accomplished by firm packing and some digital pressure. Cotton packs and rubber bands are removed. When all bleeding has stopped, the wound is thoroughly washed with warm Ringer's solution and is closed in layers. A small sandbag is placed over the dressing for about eight hours to prevent after-bleeding.

Vertebral Angiography: The technical difficulties of injecting the vertebral system are considerable because of the relative inaccessibility of the vertebral artery. Two methods are practicable. The first, elaborated by Sjöquist and King, consists of direct puncture of the vertebral artery before it enters the transverse process of the sixth cervical vertebra. Incision is made in the lower neck along the anterior border of the sternomastoid muscle at the level of the thyroid gland (Fig. 9, 2). The omohyoid muscle is exposed and divided; the sternomastoid muscle is retracted laterally. The thyroid gland is retracted medially after the sheath of the great vessels has been dissected away from its capsule. The inferior thyroid artery is retracted downward. After exposure of the deep prevertebral muscles, the transverse process of the sixth cervical vertebra is palpated. Pulsations of the vertebral artery can often be felt just below this transverse process. The deep neck muscles are then split to permit isolation of the artery for a length of about 2 cm. after being surrounded with a strip of rubber tape. It may be necessary to clip or coagulate the vertebral vein. Because of the deep position and relatively small size of the vertebral artery, its injection requires the use of a 20-gauge needle about 6 cm. in length angled 8 mm. from its point (Fig. 11). Because of the slowness of blood flow in the vertebral system, x-ray exposure is delayed for one-half to one second after the completion of injection. Eight to 10 c.c. of contrast material are sufficient.

The second method, advocated by Egas Moniz, accomplishes vertebral perfusion indirectly by retrograde injection into the subclavian artery. A transverse incision is made 2 cm. above and parallel to the clavicle, between the outer border of the sternomastoid and the trapezius (Fig. 9, 3). The external jugular vein may have to be ligated and divided. The sternomastoid muscle is retracted medially, and for good exposure its lateral margin may have to be cut. The phrenic nerve is identified and the scalenus anterior is divided. Rubber strips are placed about the subclavian artery and the thyreocervical axis. A

straight 18-gauge needle is inserted into the subclavian against the direction of blood flow and, after complete strangulation distal to the point of puncture, 10 to 15 c.c. of opaque material are injected (Fig. 12). Partial escape of the opaque material into the carotid system may occur.

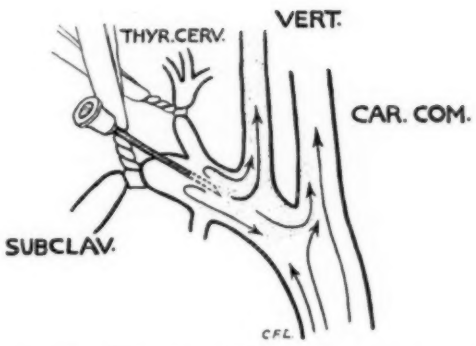


Fig. 12. Schematic drawing to show the technic of indirect vertebral arteriography. After strangulation of the subclavian artery (and thyreocervical axis), the contrast medium is injected against the current of blood into the subclavian artery. Most of the contrast medium is forced into the vertebral artery; some may flow over into the common carotid.

X-Ray Procedure

The x-ray procedure requires no specialized apparatus. It is necessary to use a tube of relatively fine focus and a moving grid to produce roentgenograms of satisfactory quality. The advantages offered by stable, well calibrated, heavy-duty equipment easily offset those provided by mobile apparatus which can be wheeled into the operating room. The equipment we have used consists of a line-focus, shock-proof tube (effective focal spot of 2.3 mm., energized by a fully rectified transformer) operating through a flat, radial type, moving Potter-Bucky diaphragm at a target-film distance of 36 inches. The tube and diaphragm are carried on a head table of the type developed at the University of Chicago (16), which is designed to permit accurate positioning and exact duplication of particular projections. This head table, though extremely convenient, is not indispensable. For lateral projections, exposures of 1.5 seconds are made at 20 ma. and 75 kv. For anteroposterior projections, kilovoltage is raised to 85 and time is increased to 3 seconds.

Our experience has shown that split-second exposures are actually less desirable than exposures as long as 1.5 seconds. The still longer exposures we have found necessary for anteroposterior projection are not desirable, but, lacking a rotating anode tube, we have been unwilling to sacrifice fine definition by employing a focal spot larger than 2.3 mm.

Stereoscopic filming is highly desirable in order to permit accurate identification of overlapping vessels as seen in lateral projection. The anteroposterior projection need not be stereoscopic, but no carotid angiogram can be considered satisfactory without a single exposure in this axis. It is important that the bifurcation of the carotid be projected above the orbits and the frontal sinuses.

By means of various types of equipment specially designed for intracranial angiography, the human factor may be largely eliminated in the spacing and timing of exposures (17, 18). It is true, however, that satisfactory results can be obtained with the apparatus already available in most hospitals.

Selection of Contrast Media

If one could discover a water-miscible substance of extreme radiopacity, entirely non-toxic and non-irritating, which, following injection, would be rapidly and completely excreted from the body, that substance would be an ideal contrast medium for intracranial angiography. While none of the materials at present available is able to meet these exacting specifications, diodrast and thorotrast are in common use.

Diodrast, which is promptly and completely excreted, produces satisfactory vessel shadows when concentrations of 35 to 60 per cent are used, but the local irritation which this material produces is troublesome and sometimes frankly alarming, especially when convulsions occur (12). Extravascular leakage produces local inflammation. In our opinion, the unde-

TABLE I: RADIOACTIVITY DETERMINATIONS

Substance	Wt. of Sample (grams)	Activity (microcuries)	Activity (mc./gram)	Computed Total Activity 44 c.c. thorotrast	30 c.c. thorotrast
Uranium standard	0.1	0.10	1.0	...	...
Thorotrast, 10 c.c. (evaporated)	4.26	0.68	0.159	2.97	2.03
Vertebra (ashed)	1.20	0.0028	0.0023	...	...
Liver (ashed)	0.068	0.0106	0.156	2.58*	1.76*
Spleen (ashed)	0.060	0.0166	0.277	0.19†	0.13†

Total measurable radioactivity, liver and spleen, after 44 c.c. thorotrast ..... 2.77 microcuries
Total measurable radioactivity, liver and spleen, after 30 c.c. thorotrast ..... 1.89 microcuries

* Wet weight of liver, 1,510 grams. Total ash, 16.61 grams.
† Wet weight of spleen, 140 grams. Total ash, 0.70 gram.

sirable properties of the substance outweigh its virtues as a contrast material in this particular field.

Thorotrast, 25 per cent thorium dioxide in colloidal suspension, is water-miscible, highly opaque to x-rays, and virtually non-irritating. Once injected, however, it is excreted very slowly and in this particular it fails to meet ideal specifications. Because of its measurable and relatively long-life radioactivity, greatly prolonged retention of thorotrast in the reticulo-endothelial system has been a source of considerable concern to several authors (9, 19). The intensity of the beta and gamma radiation from this material is probably entirely too slight to be of real importance, but in samples of 25 c.c. thorotrast is said to emit alpha particles within minimum-maximum limits equivalent to 0.5 to 1.0 microgram of radium (20). The lowest recorded rate of activity observed in the bodies of persons with demonstrable radium poisoning is that which is equivalent to 2.0 micrograms of the element (9).

One of our patients, who had an inoperable brain tumor, died several weeks after angiographic examination. Blocks of liver, spleen, and bone were obtained at autopsy. One month after death and approximately two months after angiography, these tissues were ashed, and weighed samples were submitted to Prof. James M. Cork of the Department of Physics of the University of Michigan for ionization measurements. The results of his analysis are shown in Table I. One of the injections necessary to prepare a complete set of angiograms was repeated because of inaccurate timing of the x-ray exposure, bringing the total amount of thorotrast used in this particular case to 44 c.c., whereas it should not be necessary to exceed 30 c.c. Figures in Table I show that 10 c.c. of a thorotrast sample selected at random showed a rate of radioactivity above the range reported by other authors. The ionization measurements indicate that the bulk of the thorotrast had been deposited in the liver and spleen at the time of the patient's death; that the total radioactivity of these two organs was, in this case, in excess of the lowest recorded level in cases of radium poisoning. By adjusting these figures to conform to the situation which would have obtained if the amount of thorotrast injected had been held to the recommended limit of 30 c.c., it is found that the total measurable ionization in spleen and liver would have been 1.89 microcuries, definitely below the lowest level which has been observed in radium poisoning. Contact exposures of non-screen x-ray film to samples of the spleen ash for seventeen hours produced clearly recognizable blackening on development. Blackening was very intense for longer exposures. Much fainter photographic changes were produced in the case of ashed liver, while the radioactivity in bone ash was too weak to be clearly demonstrated by the photographic method.

The potentiality of long delayed radiation damage following the intravascular injection of thorotrast in the amounts required for intracranial angiography is admittedly worrisome. In our experience the blandness of this contrast material, in

so far as immediate effects are concerned, has been well established in comparison with 35 per cent diodrast. This is a most commendable characteristic. During the three and one-half years we have been using thorotrast, none of our patients who have survived their intracranial lesions has shown any detectable signs of ill effect due to stored radioactive substances. The possibility of such undesirable effects presenting themselves at some future time cannot be denied but Egas Moniz (21), whose experience covers a period of thirteen years, has recently written us that he has never observed any suggestion of untoward effect chargeable to thorotrast.

Another contrast substance, colloidal tri-iodo-ethyl-stearate, described by Degkwitz (22), is reported by Häussler (23), to possess the desirable properties of excellent radiopacity, compatibility, and of complete elimination. This substance cannot be obtained in this country and our efforts to have it manufactured have thus far been fruitless.

DISCUSSION

When the indications for its use are clear, intracranial angiography may be employed without danger to the patient if certain conditions are observed. In our series of 127 patients examined by this method, there has been no fatality attributable to the procedure. It is manifestly unwise to inject any material into the circulation of the brain in cases of extreme arterial hypertension, far advanced arteriosclerosis acute intracerebral or subarachnoid hemorrhage, recent thrombosis, or embolism of cerebral vessels. Even in the absence of such contraindications, one may occasionally encounter transient hemiparesis, hemiparesthesia, aphasia, convulsive manifestations, or temporary accentuation of presenting neurological signs. Untoward effects such as these occurred in less than 3 per cent of our patients, and in no instance did the undesirable effects persist. Similar symptoms are fully as common after pneumographic procedures. Actually angiography is better tolerated than ventriculography in certain cases of expanding lesions associated with high intracranial pressure, because intracranial hydrodynamics are not materially altered.

Obviously, angiographic methods should be used with discretion. Preliminary lateralization of the lesion is essential if one is to know which side to inject. Carotid injection serves no good purpose if the lesion lies in the posterior fossa.

Transcutaneous arterial injection, advocated by some authors (10), does not appeal to us. We prefer the direct surgical approach, which eliminates the likelihood of extravascular leakage and inadvertent dislodgment of the needle with consequent danger of uncontrolled bleeding. Egas Moniz uses the simple surgical procedure of exposing the common carotid at the base of the neck. We feel that it is only slightly more difficult to prepare the internal carotid for injection and that this approach holds the total amount of contrast material needed at a minimum and obviates annoying shadows cast by branches of the external carotid.

SUMMARY

1. The opacification of intracranial vessels for the purpose of accurately localizing lesions within the cranium is a practicable procedure.

2. Intracranial angiography demands the employment of an exacting technic combining surgical and roentgenographic procedures.

3. Despite its undesirable property of long half-life radioactivity, thorotrast in amounts not exceeding 25 to 30 c.c. is the most satisfactory contrast material at present available for intracranial angiography.

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Roentgen Observations on Primary Atypical Pneumonia[1]

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APPROXIMATELY ten years ago scattered reports began to appear in the foreign literature concerning certain lobular pneumonias of atypical character and distribution associated with unusual clinical findings. Later reports appearing in the American literature (Bowen, Allen, Reimann, Goodpasture and others) established the disease as a new clinical entity of characteristic symptomatology, course, and laboratory findings.

Excellent discussions of the clinical and roentgen findings in this disease are to be found in the recent medical literature, but certain features, it is believed, have either escaped notice or have not received the attention they deserve.

The observations which are the subject of this paper are derived from a study of approximately 1,500 pneumonia patients admitted to the AAF Regional Station Hospital of the Santa Ana Army Air Base over a period of two years. Of these, approximately 1,200, or 80 per cent, have been clinically classified as suffering from "primary atypical pneumonia." All have had interval roentgen studies. For the purpose of accurate analysis, the roentgen findings in 300 of these cases have been carefully tabulated.

CLINICAL ASPECTS

One of the most striking features of primary atypical pneumonia, at least to the radiologist, is the relatively mild clinical course of the disease as compared with the amount of infiltration shown on corresponding chest films. In one series of 26,448 routine 4 × 10-inch photoroentgen examinations of the chest on supposedly healthy young adults applying for air crew training, 153, or 0.58 per cent, showed varying degrees of infiltration, usually small in amount, but occasionally occupying as much as one-fourth of a lung field. The findings were confirmed by recheck 14 × 17-inch films, and the subsequent clinical classification was almost invariably primary atypical pneumonia. When questioned, many of these men reported no symptoms of any kind. Others complained only of a recent "cold" or "cough" or of feeling weak, easily fatigued, or "under par."

Patients admitted to the hospital because of a more acute or severe illness complained primarily of fever and chills, cough, general malaise, weakness, and various aches and pains. The onset was usually moderately acute over a period of one to three days. Cough, either dry or productive of slight mucoid sputum, was present in most cases, and was often the outstanding symptom, complained of bitterly because of its persistent, irritating character. A sensation of extreme weakness, fatigue, or exhaustion was one of the most pronounced and also one of the commonest findings. In mild cases, it was sometimes the only symptom. There was often accompanying moderately severe and persistent headache, general aching, or both. Sore throat was frequently present but was seldom severe or the presenting symptom. Chills or chilly sensations and profuse perspiration were encountered commonly, especially in the early stages of the disease. Nasal obstruction or discharge was also observed in some cases. Pain in the chest, which was an occasional complaint, was seldom pleuritic in character but was usually of a dull or burning central type.

The incidence of these various findings in a sample group of 40 cases was as follows:

Cough (dry or productive of slight sputum)	75%
General malaise, fatigue, weakness	68%
Sore throat (usually mild or moderate)	58%
Headache (usually mild or moderate)	42%
Chills (and "chilly" sensations)	38%

[1] Accepted for publication in October 1944.

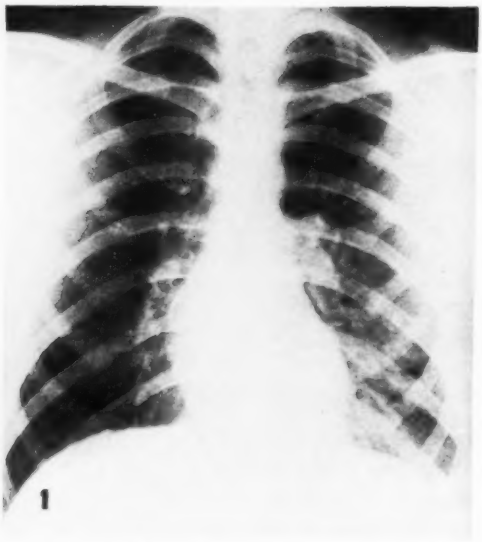

Fig. 1. Primary atypical pneumonia, mediobasal peribronchial type. Complaints: Weakness, fatigue, vertigo, anorexia, cough, initial headache, substernal oppression. Left basal râles. Temperature: 101°, two days; 99° two days. WBC: 7,400; neutrophils, 62 per cent. Sputum: Negative for pathogenic organisms.

General aching (including backache)	25%
Profuse perspiration	15%
Nasal obstruction and discharge	8%
Nausea and anorexia	8%
Pain in chest (usually central type)	5%

Physical findings were few and inconstant. In general, the patients appeared rather lethargic, apathetic, and not particularly concerned about their illness nor interested in their surroundings. Respiration was quiet and unlabored. The skin was usually warm and moist at the onset, often slightly flushed, occasionally cool, pale, or faintly cyanotic, or was changeable from day to day, particularly over the extremities, giving the impression of vasomotor instability. Inspection of the throat commonly showed a dry, unedematous erythema of mild to moderate degree. Percussion and auscultation often gave negative findings for the first twenty-four to forty-eight hours, but fine crackling râles could usually be heard over the area of involvement thereafter.

Temperature was of a spiking, irregular type, varying from 99° to 104°, usually over a period of three to six days. In only 8 patients, or 20 per cent of a sample group of 40, was the temperature elevated beyond a week. White blood counts varied from 4,450 to 17,950, with 92 per cent falling between 5,000 and 13,000. Polymorphonuclear leukocytes accounted for less than 75 per cent of white cells in 77 per cent of cases. Smears and cultures of the sputum significantly showed only the normal nasopharyngeal bacterial flora with pathogenic organisms either absent or present in insignificant numbers.

Although the acute phase of the disease was usually brief, the average period of hospitalization was approximately three weeks, often followed by convalescent care for another two to six weeks. One reason for such prolonged hospitalization is found in the persistent asthenia which so commonly follows the disease, often associated with an elevation of the pulse rate and abnormal cardiac response to exercise. An additional reason for prolonged hospitalization and convalescent care is the pronounced tendency to relapse and, in some cases, to the development of new zones of pulmonary infiltration if the patient is returned to duty too soon.

ROENTGEN FINDINGS

The infiltrations radiographically demonstrated in primary atypical pneumonia show great variation as regards extent, character, and duration. It would be difficult, in fact, to establish roentgen criteria for a "typical" case. It is even more difficult, in a given case, to decide from the film alone whether a pneumonic infiltration falls within this category. Certain general statements, however, appear justified. It can be stated, for instance, that pneumonias of this type are rarely lobar in character or distribution; that the majority are localized to the middle or lower lung fields; that they are slow in resolution, usually passing through an intermediate stage of peribronchial infiltration and occasionally shifting from one part of the lung to another; that there are few com-

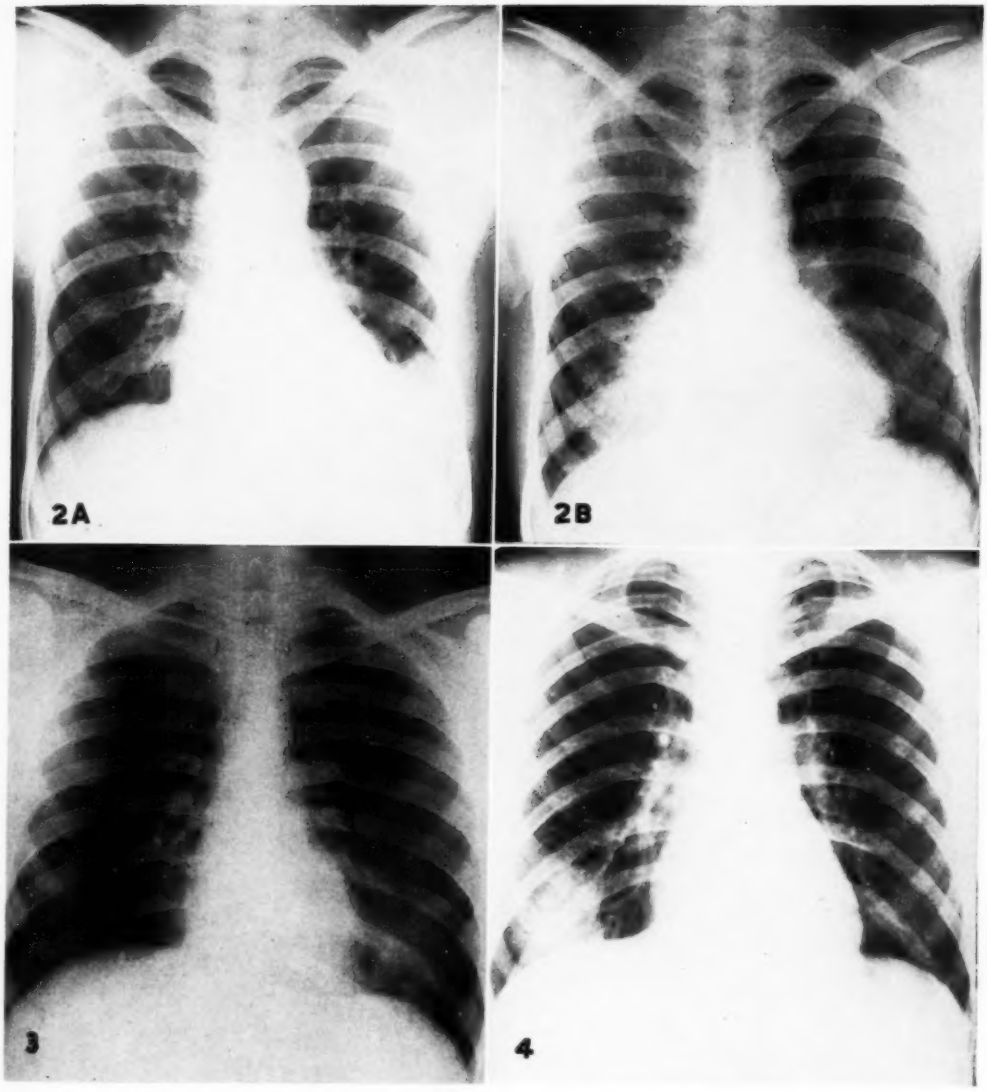

Fig. 2A. Primary atypical pneumonia, local rounded zone of consolidation, left base. Complaints: Cough, fever, general aching, pain in left chest and left shoulder on cough. Friction rub and râles, left base. Temperature 99–100°, four days. WBC: 7,500; neutrophils, 65 per cent. Sputum: Negative.

Fig. 2B. Primary atypical pneumonia, confluent, right mediobasal. Same case as 2A, six weeks later. Temperature normal during interval between development of the basal consolidations on opposite sides. The second consolidation developed when the patient was allowed a three-day pass after apparent recovery from his initial illness. Temperature: 102–104°.

Fig. 3. Primary atypical pneumonia with pneumatocele adjacent to the cardiac apex. Complaints: Chills and fever, slightly sore throat. Physical findings negative. Temperature: 99–102°, five days. WBC: 7,850; neutrophils, 76 per cent. Sputum: Negative. Pulse elevated two weeks after return of temperature to normal: at rest, 84–96; after exercise, 124–140.

Fig. 4. Primary atypical pneumonia, isolated rounded zone of consolidation, right base. Complaints: Weakness and malaise, chills and fever, slightly sore throat, cough. Râles, right base. Temperature: 99–100°, two days; normal to 99°, five days. WBC: 7,800; neutrophils, 69 per cent. Sputum: Negative. Vasomotor instability, cold moist hands, tremor, approximately five weeks.

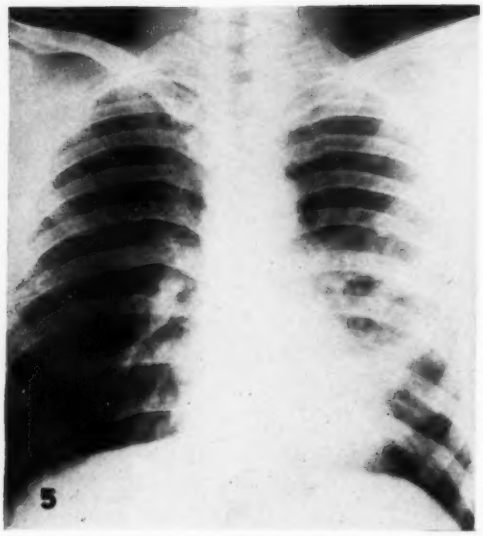

Fig. 5. Primary atypical pneumonia, hilar or central type. Complaints: Fever, aches and pains, slight headache, general malaise, slightly productive cough. Few râles in left axilla. Temperature: 99–100°, five days. WBC: 8,700; neutrophils, 61 per cent. Sputum: Negative.

plications; and that a fatal termination is rare indeed.

Infiltrations of primary atypical pneumonia fall roughly into two main classes: one, a mediobasal peribronchial type; the other, a more or less confluent type of pneumonic consolidation. Of our sample group of 300 cases in which the roentgen findings were tabulated, 110, or 37 per cent, were of the peribronchial type, while the remaining 190 were classified as the confluent type of pneumonia.

The peribronchial type of infiltration is localized, in the great majority of cases, to the mediobasal portions of the lungs. It varies in extent from a fuzzy thickening of the mediobasal trunks with haziness of intervening tissues to a diffuse patchy or mottled involvement, again closely associated with the basal trunk markings. In general, these cases comprise the clinically milder, more rapidly resolving pneumonias, though infiltration may persist one to three weeks after the temperature returns to normal and the patient feels clinically well. The average time required for clearing in 110 cases was between two and three weeks.

We have two cases with presumptive evidence that bronchiectasis developed following a peribronchial atypical pneumonia. Coughs which initially occurred with the acute phase of the disease in these patients persisted and increased. Previous histories were entirely negative as regards the chest. Lipiodol bronchograms revealed a definite bronchiectasis of mild to moderate degree in each case. Recheck bronchograms taken on one of the patients, however, showed the bronchiectasis to have practically disappeared along with clinical symptoms after a period of approximately four months.

Frank consolidations of the confluent or relatively homogeneous type accounted for 63 per cent of our sample group of 300 cases. Most of the clinically more severe or prolonged cases fall within this group, but many mild cases are also included.

A large majority of the pneumonic infiltrations are found in the middle or lower lung fields. Among the 190 confluent pneumonic cases in our series, the distribution in the lung fields was as follows: right lower, 63; left lower, 76; bilateral lower, 6; hilar and mid-lung, 28; right upper, 15; left upper, 2. The infiltrations vary from a soft homogeneous veil-like haze to a density of moderate grade, approaching, but rarely equalling, that of lobar pneumonia. They frequently assume a rounded shape somewhat denser in the center, fading at the periphery. Occasionally well circumscribed rounded zones of consolidation are encountered which appear almost ball-like in the lung fields. True lobar distribution is seen only rarely; the disease is no respecter of interlobar boundaries. Nor, as a rule, is the infiltration so uniform as in lobar pneumonia, though large confluent cotton-woolly zones are common. Occasionally (2 per cent in our series) central pneumatoceles develop within zones of consolidation, producing cavity-like appearances. Such pneumatoceles disappear as the surrounding pneumonia resolves.

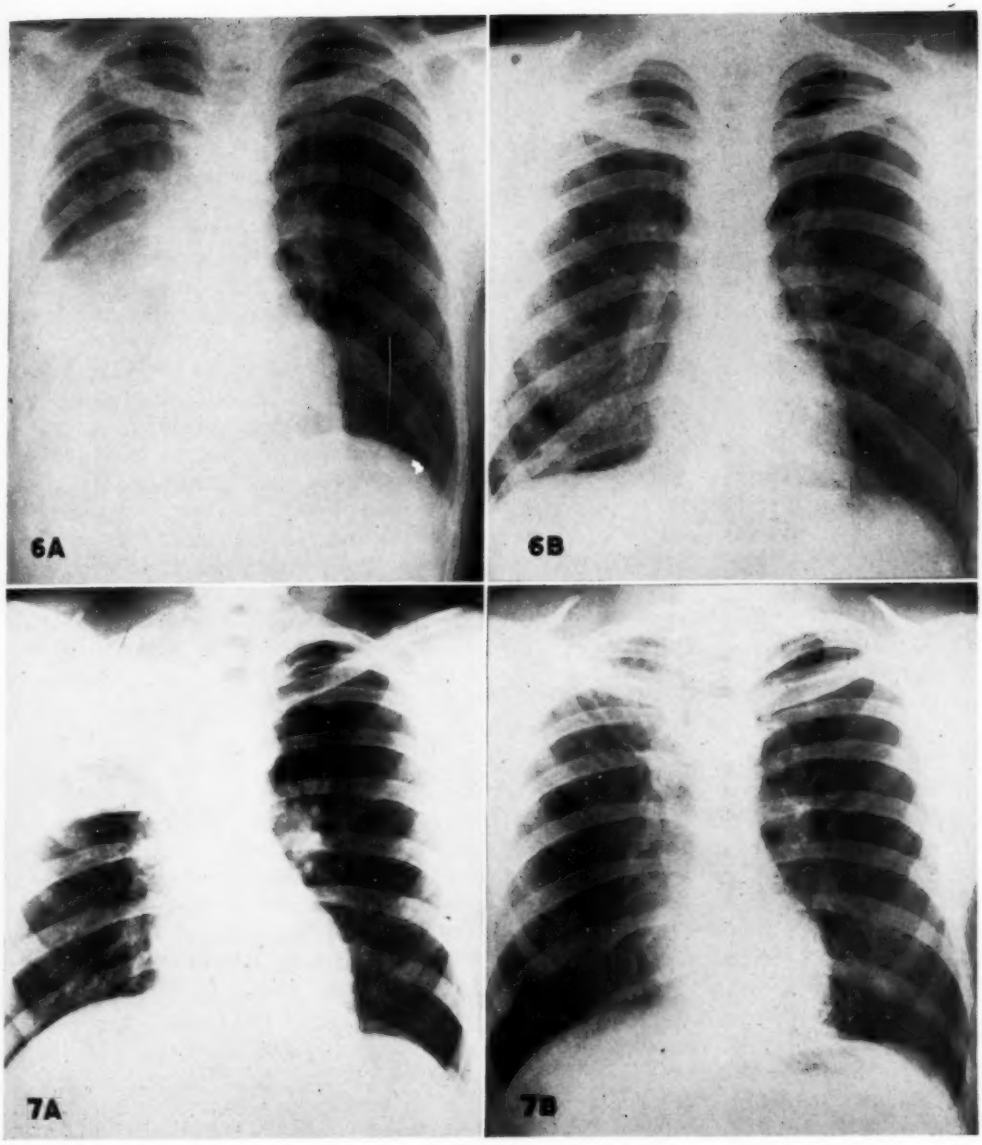

Fig. 6A. Primary atypical pneumonia, extensive, involving primarily right middle and lower lobes. Complaints: Fever, chilly sensations, dry cough, headache. No râles until two days after admission. Temperature: 99–103°, eight days. WBC: 8,750; neutrophils, 65 per cent. Sputum: Negative.

Fig. 6B. Primary atypical pneumonia, in peribronchial stage of resolution. Same case as 6A, ten days later. After an additional two weeks, the lungs had cleared completely.

Fig. 7A. Primary atypical pneumonia involving right upper lobe. Complaints: Cough, substernal pain, headache. Friction rub, right sternal border. Râles not heard until fifth day. Temperature: 100–103°, ten days. WBC: 8,500; neutrophils, 65 per cent. Sputum: Negative.

Fig. 7B. Primary atypical pneumonia in peribronchial stage of resolution. Same case as 7A, one week later. The appearance at this stage is suggestive of pulmonary tuberculosis. The lungs were completely clear after three weeks.

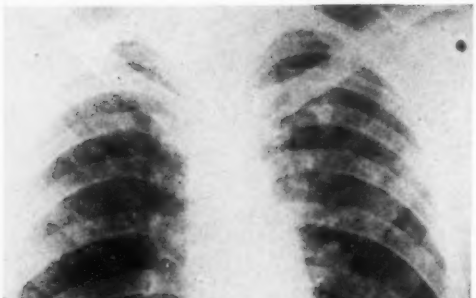

Fig. 8. Primary atypical pneumonia, diffuse, finely patchy type. Onset abrupt with severe malaise, chills, cough, moderately sore throat. Patient severely ill; course not affected by sulfa drugs, convalescent serum, or other therapy. Temperature: 100–104°, eighteen days. WBC: 11,650; neutrophils, 78 per cent. Sputum: Negative. Right brachial peripheral neuritis developed on the twenty-fourth day of the patient's illness.

Considerable emphasis has been placed by some observers on the hilar type of atypical pneumonia, certain ones going so far as to imply that all primary atypical pneumonias are primarily hilar in origin. This has not been our experience, though a majority of cases (62 per cent) do show at least partial hilar involvement. In 38 per cent of our series infiltration appeared entirely separate from the hilum during the entire course of the disease.

Atypical examples of the disease are occasionally encountered, which simulate pulmonary tuberculosis, coccidioidomycosis, lobar pneumonia, or other conditions. Isolated patches appearing at the apices resemble the acute exudative type of adult tuberculous infection. During the resolution stage, infiltrations in this region may simulate the proliferative phase of tuberculous involvement. Rapid and complete resolution of the inflammatory process will, of course, readily establish the true diagnosis. In 4 of our sample group of 300 cases infiltrations were so situated and of such character as to require observation over a period of two to three weeks in order to rule out the possibility of tuberculosis. In 2 additional cases, infiltration was of a finely nodular or patchy type, scattered uniformly in both lungs in such a fashion as to require differentiation from miliary tuberculosis, silicosis, or other miliary disease. The clinical course in both these cases, incidentally, was unusually severe and prolonged, but the infiltrations cleared, leaving no trace in the lungs.

Isolated nodular zones of consolidation, especially if small and well circumscribed, may simulate corresponding lesions of coccidioidomycosis but are readily differentiated clinically and by the rapid resolution of the former. The pneumonic type of acute primary coccidioidomycosis, however, may be indistinguishable both clinically and radiographically, except for specific dermatologic and serologic tests in the latter.

Two of our cases presented appearances which, from the films alone, could not be readily differentiated in their initial phases from true lobar pneumonia. In one case uniform consolidation was limited to the right upper lobe; in the other, it occupied the right middle and lower lobes. The clinical and laboratory findings, course, and resolution, however, were so different from those of lobar pneumonia that diagnosis was no problem.

A small percentage of pneumonic consolidations of the primary atypical variety clear uniformly and rapidly in a matter of days, resembling, in this respect, the resolution of lobar pneumonia. But in over two-thirds resolution is a slow, gradual process, requiring a period of two to six weeks. In a typical case, consolidation, which is at first of a confluent, almost homogeneous type, gradually loses its density, becomes mottled, then patchy, finally peribronchial. The peribronchial stage is usually seen beginning about the second week of the disease and lasting until its termination some one to six weeks later. The infiltration at this stage resembles that of the milder cases which, during their entire

course, never progress beyond this point. It is unusual, however, to find a pneumonic infiltration which initially appeared to be of a peribronchial type, progressing to confluent consolidation.

An interesting feature of the disease is its tendency to shift from one lung area to another. It not infrequently happens that as the initial pneumonic infiltration is clearing in one location, an entirely new zone of infiltration will appear in an unrelated lung area, frequently on the opposite side. In some instances, the newly developed consolidation will appear after complete resolution of the initial lesion, as in those patients who are allowed up too soon following the acute stage of the illness. These secondary infiltrations are similar in character and duration to the initial involvement and undergo an independent evolution.

Complications are rare in primary atypical pneumonia. In only 3 of our sample group of 300 did pleural effusion develop, and this in such limited amount as scarcely to fill the costophrenic angle. In 2 cases infiltrations failed to clear completely and after the third month presented an interlacing strand-like appearance characteristic of interstitial fibrosis. The single death in the entire series of 1,200 patients resulted from a secondary ascending myelitis which developed on the eighth day of illness. The appearance of the lung consolidation preceding and accompanying the myelitis was in no way remarkable, and the clinical course and laboratory findings prior to its development were not unusual.

PATHOLOGY

In the few cases of primary atypical pneumonia coming to autopsy, the pathologic findings have been primarily those of an interstitial pneumonia with accompanying destructive or degenerative changes in the alveolar and bronchial epithelium. The interalveolar septa have been described as thickened by hemorrhage and edema, and the interstitial tissues have been crowded with lymphocytic and monocytic cells, while relatively few neutrophils have been present. Adams and Goodpasture found characteristic inclusion bodies in bronchial epithelial cells.

In the single fatal case occurring in our series, destructive and degenerative changes were a prominent feature, interstitial changes were extensive, and neutrophilic leukocytes were numerous. The histopathologic findings were described by the pathologist as follows:

"The lumens of the terminal bronchi are filled by fibrinopurulent exudate, the elements of which are partially degenerated and occasionally diffusely necrotic. Frequently the bronchial epithelium is necrotic. Walls of the bronchi are edematous and infiltrated by neutrophilic leukocytes. Proliferation of their connective-tissue elements is often conspicuous. Vacuolization of the smooth-muscle cells of the bronchi and arteries is common. Some groups of adjacent alveoli contain fairly well preserved fibrinopurulent exudate, and in others this has been replaced by masses of proliferative connective-tissue cells and capillaries. Occasional groups of alveoli have lost identity and are replaced by amorphous eosinophilic material and nuclear debris. The numerically predominant cell of the exudate is the neutrophilic leukocyte, but large mononuclear phagocytic cells are also encountered. The septa in the areas of consolidation are thickened by exudative and proliferative inflammatory changes. Lymphatic channels are rendered conspicuous by networks of fibrin. Gram-Weigert, Giemsa, methylene blue and carbol fuchsin stains do not aid in identification of bacteria. No inclusion bodies are found."

TREATMENT

The treatment of primary atypical pneumonia consists primarily of prolonged bed rest and symptomatic management of cough, headache, sore throat, and other complaints as they arise. Sulfa drugs are not of value and are contraindicated unless secondary bacterial infection is suggested by sputum studies, excessively high white

blood count, or unexpected complications. Convalescent plasma has been used in approximately 75 of the more severe cases at the Santa Ana Army Air Base with some evidence that it is of value early in the course of the disease.

SUMMARY

1. Of a series of approximately 1,500 pneumonia patients admitted to the AAF Regional Station Hospital of the Santa Ana Army Air Base over a period of two years, about 1,200 or 80 per cent have been clinically classified as primary atypical pneumonia.

2. Clinically, one of the most striking features of the disease is the relatively mild symptomatic course as compared with the amount of lung consolidation shown on corresponding chest films. Many ambulatory patients are discovered to have the disease by routine screening films. Prolonged convalescent care is required in many cases because of persistent postpneumonic asthenia.

3. A normal or depressed white blood count and absence of pathogenic organisms in sputum cultures are among the most significant of laboratory findings.

4. The radiographically demonstrated pulmonary infiltrations fall roughly into two main groups: one, a comparatively mild mediobasal peribronchial type of infiltration; the other, a more or less confluent type of pneumonic consolidation. Unusual types may simulate adult reinfection tuberculosis, miliary tuberculosis, coccidioidomycosis, lobar pneumonia, and other diseases. The majority of pulmonary consolidations are localized to the middle or lower lung fields. They are slow in resolution, usually passing through an intermediate peribronchial stage and occasionally shifting from one lung area to another. There are few complications, and a fatal termination is rare.

5. In the single death in our series, interstitial inflammatory changes in the involved lung tissues were outstanding, and degenerative changes in the bronchial and alveolar walls were a prominent feature.

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The Roentgen Appearance of Lobar and Segmental Collapse of the Lung

III. Collapse of an Entire Lung or the Major Part Thereof

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THE PURPOSE of this paper is to present certain signs which are of value in the recognition of collapse of an entire lung, or the major part thereof. Because of the existing confusion in the use of the terms "collapse" and "atelectasis," we have arbitrarily chosen "collapse" to mean a decrease in size and "atelectasis" to indicate airless alveoli which are smaller than normal. No attempt will be made to discuss the etiology of collapse.

From a total of approximately 85,000 chest examinations conducted at the Massachusetts General Hospital during the past seven years, we reviewed in detail 1,200 in which a diagnosis of tumor, bronchiectasis, foreign body, or tuberculosis was made. After discarding the cases in which the roentgenograms were inadequate (films in two projections, the posteroanterior and lateral, being considered the minimal requirement for determining the size of a lobe or its segments), approximately 600 remained in which at least one lobe was less than two-thirds of its normal size. Only collapse produced by intrinsic disease of the lung was included; collapse attributable to extrinsic factors, as pneumothorax, pleural fluid, or a pleural tumor, was excluded.

Analysis of this group of 600 cases revealed that collapse was limited to a single lobe, or segment, in 71 per cent, that it involved two or more lobes in 18 per cent, and was massive in 11 per cent. Collapse of the left lung was more frequently observed than collapse of the right lung. The various lobes were involved as follows: left lower lobe, 42 per cent; right lower lobe, 26 per cent; right middle lobe, 26 per cent; left upper lobe, 8 per cent; right upper lobe, 8 per cent. The percentage of cases with extensive collapse would have been greater had all the cases in which massive collapse followed operative procedures been included. In many of these patients, however, examination was limited to a single portable roentgenogram, which was insufficient to warrant their inclusion in this study. Since our present interest is to describe as accurately as possible the findings in collapse of an entire lung, or the greater portion of a lung, a group of 30 cases in which the requisite number of roentgenograms were available was selected as a basis for our conclusions. Detailed description of collapse of the various lobes will be presented in subsequent papers.

Collapse of an entire lung, whether it be acute or chronic, usually shows the characteristic roentgenologic signs by which collapse has long been recognized (1*b*, 2, 3, 4): an abnormal shadow of increased density, elevation of the diaphragm, displacement or shift of the mediastinum, and narrowing of the rib spaces.

In acute collapse of the lung, the shadow of increased density is as a rule homogeneous, indicating complete atelectasis, although certain segments of some lobes may not be atelectatic. The structure of the involved lung, including the hilar shadow and septa, is obscured. The side of the chest which contains the collapsed lung is more radiopaque than the opposite side, due to increase of soft-tissue density per unit volume without air, whereas the density of the uninvolved side is diminished as a result of compensatory emphysema. The shadow of increased density, representing collapse of the greater portion of a lung, may at first glance be confused with

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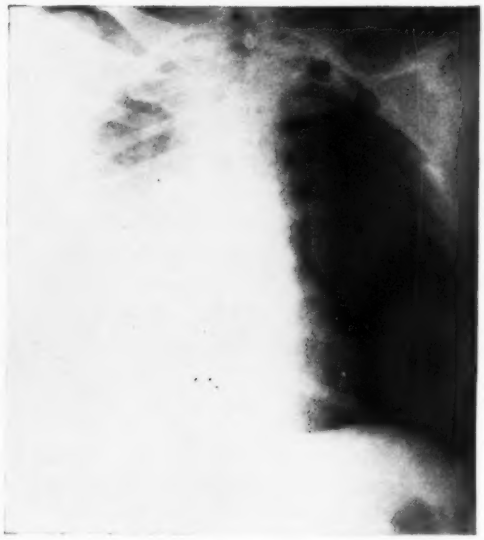

Fig. 1 (portable roentgenogram). Acute collapse of the right lung four days following subtotal gastrectomy. The shadow of increased density appears to involve the greater portion of the right lung. The heart and mediastinum are displaced to the right. The rib spaces are questionably narrowed. The position of the diaphragm is not definite. A roentgenogram taken five days later showed the lung considerably re-expanded.

pneumonia or pleural effusion. Pleural effusion, however, is a space-consuming lesion which displaces the lung, the mediastinal contents, and the diaphragm, producing a shadow which is often larger than the area usually allocated to the lung; while pneumonia may produce a homogeneous shadow of increased density but little or no change in the size of the lung.

The mediastinum is displaced toward the collapsed lung and shows, during fluoroscopy, a definite inspiratory shift to the side of the lesion. The amount and type of displacement of the mediastinal contents are essentially the same regardless of which side of the chest is involved. The adjacent border of the heart is obscured by the shadow of density, and fluoroscopically the pulsations in this area are usually invisible. If the diaphragm is visible, it is seen to be elevated and ordinarily shows some limitation of motion during fluoroscopy. Since in most cases its upper surface is obscured by the shadow of increased density, determination of its position will depend on demonstration of its lower surface, particularly on the left side. This can be done easily when the diaphragm is outlined by underlying gas in either the stomach or colon. If this is not the case, demonstration of the fundus of the stomach with barium will usually show the position of the diaphragm. The right side is much more difficult to localize accurately, but if there is no reason to assume abnormality in the size of the liver, a suggestion of the position of the diaphragm can be gained by locating the inferior margin of that organ. The rib spaces as a rule appear to be narrowed on the side of the chest involved.

If it is borne in mind that the last three signs of collapse are all the result of a *decrease in size* of the involved lung, collapse of a lung is less likely to be confused with pneumonia, pleural effusion, or other disease process.

In chronic collapse of the lung, the shadow of increased density could not, in some instances, be differentiated from that seen in acute collapse, whereas in others it became so small that it was difficult to recognize. The collapsed lung lies posteriorly and medially; on the left side, it is often partially obscured by the heart or other mediastinal contents, while on the right, it blends with the shadow of the diaphragm, liver, and mediastinum. The blending of the shadow of increased density with the adjacent margin of the heart makes it impossible to determine the exact size of either the heart or of the shadow of density. The mediastinum is displaced toward the side of the lesion, though fluoroscopically the mediastinal shift is usually less apparent than in acute collapse. The heart moves toward the side of the lesion and posteriorly. The uninvolved, emphysematous lung tends to herniate through the mediastinum. In our experience, this herniation has been confined to the anterior mediastinum (1*a*).

Recognition of pulmonary herniation is largely dependent upon the lateral roentgenogram, which demonstrates an increase in the distance between the sternum and

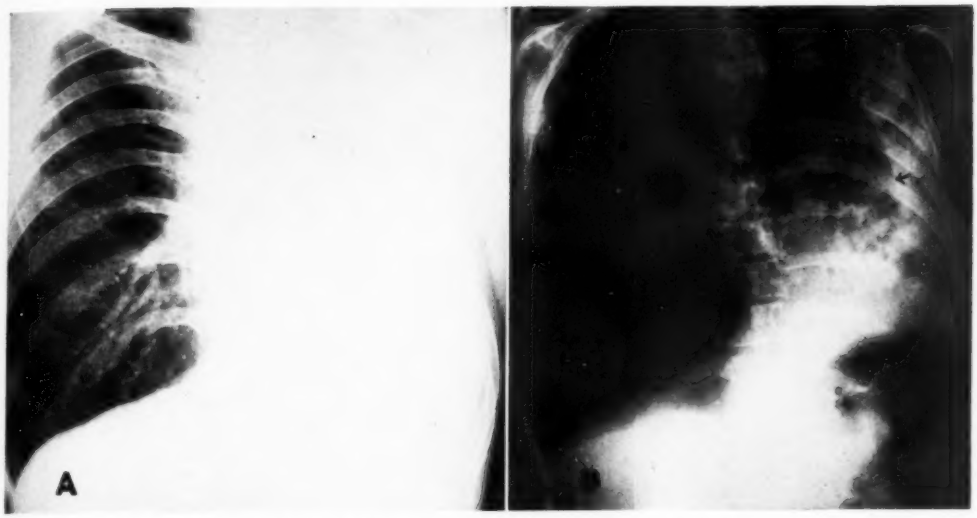

Fig. 2. Chronic collapse of the left lung due to bronchiectasis. A. Hazy density obscures the entire left lung field, and some mediastinal displacement is apparent. B. Grid film demonstrates the displacement of the trachea and mediastinum. The edge of the herniated lung is clearly seen (arrows). The bronchiectatic cavities within the left lung are visible. The approximate position of the left diaphragm is determined by the position of the gas-filled colon. See also Figure 2C.

the anterior border of the heart and the ascending aorta. In the anteroposterior Bucky and postero-anterior grid films it is usually possible to determine the margin of the herniated portion of the lung. If the hernia is small, the margin may be just beyond the mid-line, while a large hernia may extend to the lateral chest wall. The size of the hernia depends on the amount and the duration of the collapse. In some cases, it may be of such degree that the herniated, uninvolved lung may almost completely aerate the opposite chest.

The presence of a hernia is frequently not apparent until one observes the distribution of the vascular shadows. Close examination of these will reveal that there are altogether too few shadows within the herniated portion of the lung as compared with normal lung. In extreme cases of herniation, the apparent aeration by the emphysematous lung tends to create the impression that the collapsed lung is fairly well aerated. Herniation of the right lung in collapse of the left has been more frequent than the reverse. Likewise, herniations to the left side have been considerably larger than those to the right.

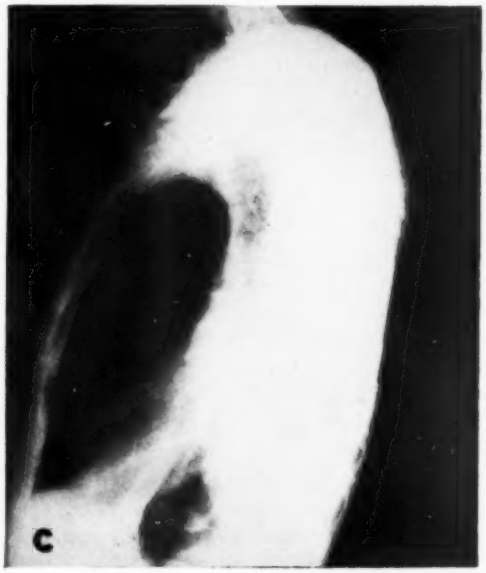

Fig. 2C. Lateral view of case shown above, showing large space occupied by the mediastinal hernia between the sternum anteriorly and collapsed lung and heart posteriorly. Total pneumonectomy performed.

In this study, a sizable hernia has been frequently observed in chronic collapse but has not been seen in acute collapse.

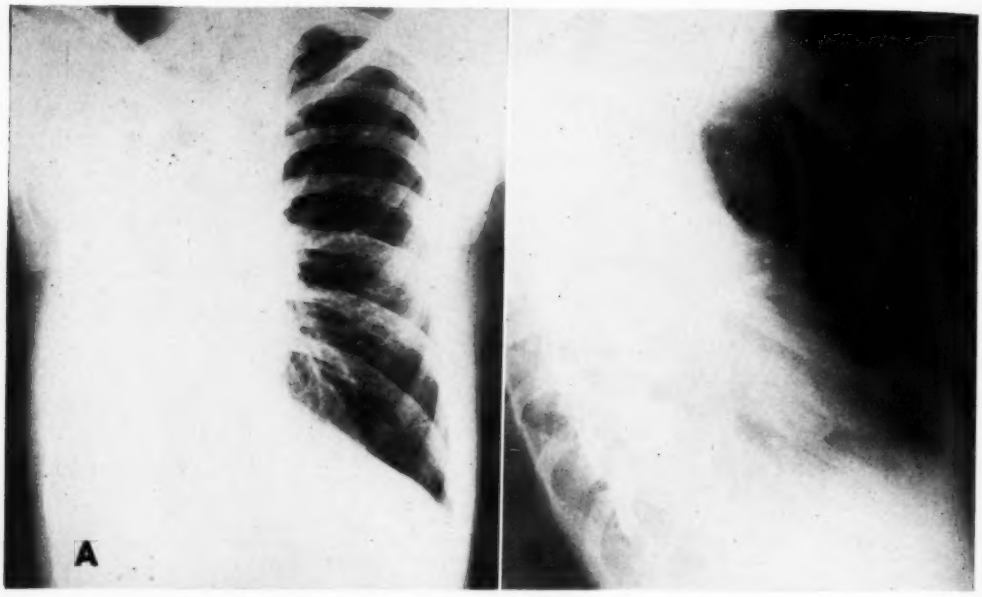

Fig. 3. Chronic collapse of the right lung due to bronchiectasis. A. Fairly homogeneous density obscures the right lung field. The heart shadow is not visible due to its marked displacement to the right. The left lung is emphysematous. B. In the lateral view, the space occupied by the mediastinal hernia is clearly visible.

Right lower lobectomy, as the first stage of a pneumonectomy, was performed. At operation, it was found that the entire right lung was collapsed. On opening the right pleural cavity, the heart shifted to its normal position immediately, and an empty space remained where it had previously been located.

The changes in the diaphragm are usually less marked in chronic than in acute collapse, because the herniated lung from the opposite side is of sufficient size to compensate partially for decrease in size of the involved lung. This factor also limits somewhat any apparent narrowing of the rib spaces. In many instances there is associated scoliosis of the dorsal spine with the convexity away from the side of the collapse. In the absence of scoliosis, or unless the onset of collapse occurred in childhood, it is doubtful if the narrowing of rib spaces is more than one would expect to find during full expiration.

The tendency of the involved side of the chest to be smaller than normal holds true for chronic as well as for acute collapse, though, because of the herniated lung, the decrease in size is generally not so great in chronic collapse. In contrast, however, the shadow of increased density is usually smaller in chronic than in acute collapse.

CONCLUSIONS

Careful study of the roentgenograms of patients suffering from collapse of an entire lung has shown two striking differences between acute and chronic collapse:

1. In acute collapse the shadow of the collapsed lung is readily seen; in chronic collapse it may be difficult to identify.

2. Herniation of the uninvolved lung through the mediastinum was a frequent finding in chronic collapse but it was not seen in acute collapse.

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Atrophy of Terminal Phalanges in Clubbing and Hypertrophic Osteoarthropathy[1]

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THE PATHOGENESIS of clubbing of the fingers and toes has remained obscure in spite of numerous investigations. Since Hippocrates' original description of this phenomenon in a patient with empyema it has been found associated with various conditions such as cardiac, pulmonary, and gastro-intestinal disease. Clubbing has been recognized as both acquired and hereditary in type and has been classified as idiopathic in cases in which an etiologic factor has not been established. Hypertrophic osteoarthropathy is now generally believed to be a more pronounced and advanced stage of the same process (1).

The bone changes occurring in hypertrophic osteoarthropathy have attracted considerable attention since the original investigations of Bamberger (2) and Pierre Marie (3). The condition is characterized by an irregular periosteal thickening of the shafts of the involved bones. In advanced stages subperiosteal new bone formation may be so pronounced as to result in marked thickening of the bone shafts and in conspicuous swelling of the involved parts. The bones most frequently affected are the long bones of the extremities, the metacarpal and the metatarsal bones, the proximal phalanges, and clavicles. The vertebrae and ribs are rarely involved.

The bone changes taking place in the terminal phalanges in simple clubbing and hypertrophic osteoarthropathy deserve special consideration. Earlier observers believed the enlargement of the distal portions of the fingers and toes to be the result of bony overgrowth (2). This conception was revised after roentgenologic studies showed the clubbing to be attributable chiefly to enlargement of the soft tissues. In most instances no changes whatsoever were observed in the terminal phalanges. Thus, Hodges, Phemister, and Brunschwig (4) claim that "almost invariably there are no bone changes of the terminal phalanges at the site of clubbing." In some cases, however, a characteristic burr-like overgrowth of the unguinal process of the phalanx was observed. Locke (1), who examined a large series of patients, noted hypertrophic changes of the terminal phalanges in 28 per cent of those with simple clubbing. Of 5 patients with advanced hypertrophic osteoarthropathy observed by this investigator, all showed hypertrophic changes of the terminal phalanges.

Mendlowitz (5), in his review of clubbing and hypertrophic osteoarthropathy, refers to a small number of cases which showed characteristic atrophic changes of the terminal phalanges. These cases are reported in the foreign literature. To our knowledge, no similar reports have appeared in the American and English literature.[2]

The recognition of these atrophic changes in clubbing and hypertrophic osteoarthropathy would seem to be of importance to the roentgenologist, in the differential diagnosis of conditions characterized by destructive changes in the terminal phalanges.

On account of the rarity of such observations, the two cases which follow were thought to merit brief description.

CASE I: E. S., a colored laundress, age 59, was seen at Grady Hospital with great enlargement of the distal portions of the ulnae, radii, tibiae, and fibulae, as well as broad clubbing of the soft tissues

[1] From the Departments of Roentgenology and Medicine, Grady Hospital and Emory University School of Medicine. Accepted for publication in October 1944.

[2] Since preparation of this paper we note that a case similar to our Case II has been described in the recently published handbook, *The Arthropathies*, by A. A. de Lorimier, Year Book Publishers, Inc., Chicago.

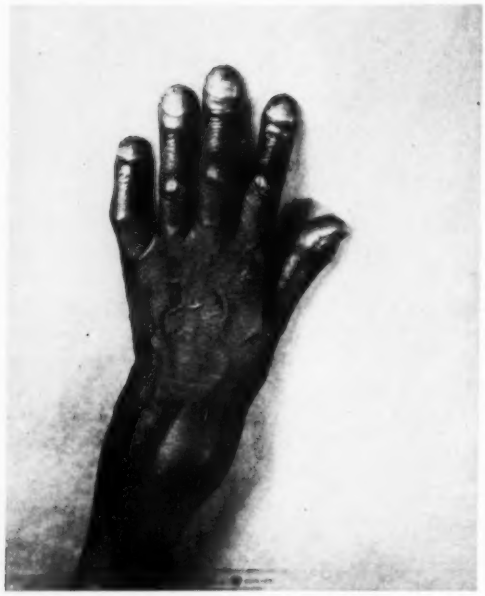


Fig. 1. Case I: Left hand, showing clubbing of fingers and swelling of distal forearm.

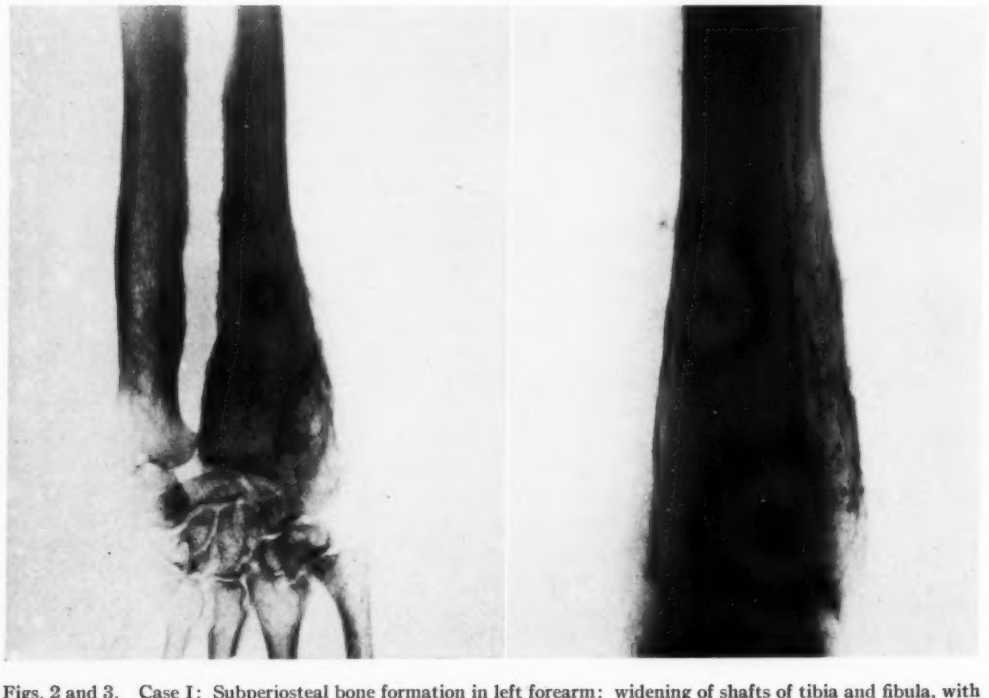
of the distal segments of all digits (Fig. 1). She showed flexion deformity of the hands due to limitation of extension at the enlarged proximal interphalangeal articulations. These enlargements were virtually free from pain, although there was arthralgia in some other joints.

The patient stated that these enlargements had been present all her life, and had been a source of childhood nicknames, but she believed there had been progression of enlargement in the past twelve years.

She showed no cyanosis, had normal peripheral pulses, and presented no sign or history of cardiorespiratory or other chronic disease. None of her seven siblings had similar osteoarthropathy.

Laboratory studies recently showed insignificantly mild normochromic anemia, normal urine, and a normal serum calcium level.

Roentgen Examination: The distal portions of radius, ulna, tibia, and fibula on both sides showed marked widening of the shafts (Figs. 2 and 3). There was extensive formation of subperiosteal cancellous bone with apparent absorption of the original cortex. Small irregular spurs protruded from the surface of the involved bones into the soft tissues. These changes were also observed in the fifth metatarsal bones. The remaining metatarsal bones, the metacarpal bones, and the proximal phalanges had



Figs. 2 and 3. Case I: Subperiosteal bone formation in left forearm; widening of shafts of tibia and fibula, with thick layers of subperiosteal bone.

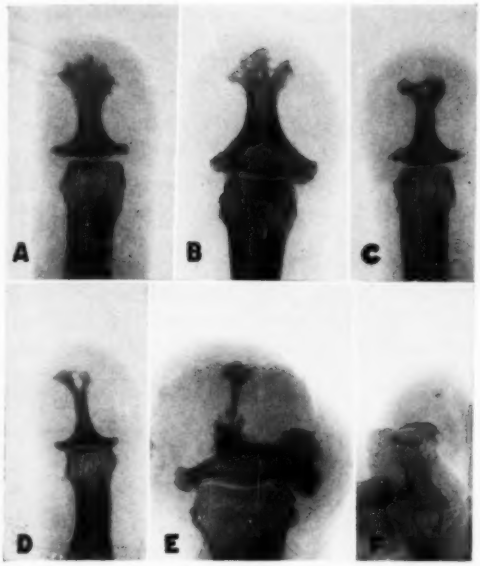


Fig. 4. Case I: A. Right 3d finger. B. Right 1st finger. C. Right 4th finger. D. Left 5th finger. E. Right 1st toe. F. Left 5th toe. Hypertrophic changes are shown in A, while various stages of atrophy are seen in B to F.

the usual appearance. The middle phalanges of the toes showed a thinning of the shafts. Characteristic atrophic changes of varying degree were observed in the terminal phalanges of the fingers and toes (Fig. 4, B–F).

CASE II: C. M., a colored male, was said to have been a "blue baby" at birth. He was always easily fatigued, and when he was seen at the age of 14 years at Grady Hospital for syncopal attacks and dyspnea, a diagnosis of "congenital heart disease with cyanosis" was made. On the basis of physical examination, blood chemical studies, and roentgen examination, the accepted clinical diagnosis was "tetralogy of Fallot."

In his terminal illness, at the age of 30 years, when he presented the clinical picture of recurrent cerebral embolism, he was cyanosed, aphasic, and decompensated, with typical soft-tissue clubbing of the distal digital segments without evidence of osteoarthropathy. Autopsy was not permitted.

Roentgen Examination: The unguinal processes of the terminal phalanges of the toes showed evidence of atrophy (Fig. 5). No bone changes were observed throughout the terminal phalanges of the fingers. The long bones revealed no hypertrophic changes.

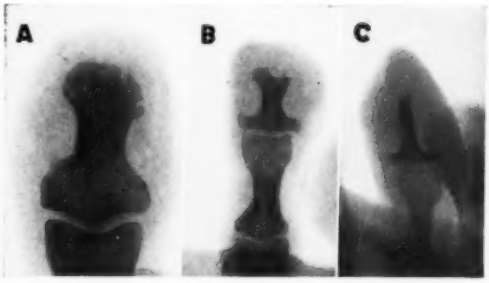


Fig. 5. Case II: A. Left 1st toe. B. Left 2d toe. C. Left 4th toe. All three roentgenograms show various stages of atrophy.

DISCUSSION

From the bone changes observed in these two cases, it can be assumed that the absorption of the terminal phalanges is preceded by hypertrophic changes. These hypertrophic changes are still well shown in the terminal phalanx of the right middle finger in Case I, the unguinal process of which shows a burr-like overgrowth (Fig. 4, A). The shaft of this phalanx appears increased in width, and there is some widening of the base. Figure 4, B to F, shows, also, various stages of atrophic change in the terminal phalanges in Case I, and in Figure 5, A to C, a similar process in Case II is illustrated. It is believed that the structural changes have taken place in the following sequence. First, a gradual splitting and notching of the unguinal process occurs, with the distal convex margin of the terminal phalanx becoming flattened and concave (Fig. 4, B and C; Fig. 5, A and B). At the same time a concentric atrophy of the shaft may be initiated so that the terminal phalanx assumes a collar-button-like appearance (Fig. 4, D and E). Finally, complete absorption of the unguinal process may give the terminal phalanx the appearance of a thumb tack (Fig. 5, C). In some instances the absorption progresses to complete atrophy of the shaft and unguinal process, so that only the base of the terminal phalanx is seen as a disk-like remnant (Fig. 4, F).

Various explanations have been offered as to the development of the atrophic changes. Lippmann (6), who observed this process in an eighteen-year-old patient with congenital pulmonic stenosis, believed that the swelling of the soft tissues, by exerting a constant pressure on the

terminal phalanges, resulted in atrophy. He arrived at this conclusion because the atrophic changes were most pronounced in those fingers and toes which showed maximum clubbing. Singer (7), who recorded a similar process in a patient with congenital heart disease, suggested local circulatory disturbance as the cause of the changes in the terminal phalanges. He noted, on capillaroscopic examination, elongation and dilatation of the small blood vessels of the fingers and toes and advanced the theory that the dilated vessels could produce erosion of the surface of the adjacent bone. The pathologic anatomic studies of Crump (8) did not confirm this conception.

Histologic and radiologic observations have demonstrated that the osseous changes of hypertrophic osteoarthropathy are not merely the result of apposition of periosteal bone. In advanced cases lacunar absorption and osteoporosis of the newly formed subperiosteal bone and underlying original bone may attain significance (9). The absorptive changes demonstrated on pathologic examination were usually studied in the long bones of the extremities. It seems conceivable that in the terminal phalanges hypertrophic changes may be followed by the same absorptive process, resulting in atrophy.

In differential diagnosis of the atrophic changes of the terminal phalanges which are described above, all conditions which are associated with destructive changes of the fingers and toes should be considered. In Raynaud's disease, scleroderma, and psoriasis, bone atrophy is usually not observed unless atrophic changes of the soft tissues have taken place. In the neurotrophic disorders, such as syringomyelia and tabes dorsalis, the tips of the fingers and toes may assume a club-shaped appearance due to inflammatory soft-tissue swelling. The destructive changes of the phalanges in leprosy are in most instances caused by a neurotrophic disturbance and resemble syringomyelia to a certain extent (10). Characteristically, the bone changes in these neurotrophic disorders are most prominent where fingers and toes are exposed to a maximum of trauma. Thus the heads of the metatarsal bones as the points of weight-bearing show most of the involvement in the form of concentric atrophy. Contrary to this finding, the atrophic changes in clubbing and hypertrophic osteoarthropathy are predominant in the terminal phalanges. It will be noted that the fingers in neurotrophic disturbances may be shortened, assuming a stubby appearance. Shortening of fingers and toes should, however, not be expected in patients with clubbing and hypertrophic osteoarthropathy.

SUMMARY

Two cases of clubbing of the fingers and toes are presented, in which the terminal phalanges show various stages of atrophy. One of these cases revealed advanced hypertrophic osteoarthropathy. The atrophic changes in the terminal phalanges are thought to have been preceded by hypertrophy, which is the bone change frequently described in this condition. The differential diagnosis of atrophy of the terminal phalanges is discussed.

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Treatment of Carcinoma of Prostate by Irradiation[1]

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PROSTATIC CANCER is recognized as one of the most frequent types of malignant growth in man. Wolff, in a review of medical literature in 1899, found only 83 recorded cases of carcinoma of the prostate. Today the literature abounds with reports of this disease and the incidence is placed at 14 to 20 per cent of all prostate tumors.

The prognosis for cure in carcinoma of the prostate is bad for two reasons: (*a*) in the early stages the disease is without symptoms; (*b*) early metastatic invasion, by perineural routes, of the pelvis, sacrum, vertebrae, and femur occurs. Hence, the curative value of early radical surgery is limited to a very small percentage of cases—according to Lowsley (1), less than 5 per cent. Formerly, the prognosis for alleviation of symptoms and any appreciable extension of life was also bad. Today it is much better. That this improvement is due to a more alert understanding of the influence of certain male hormonal substances on the cellular structure of prostatic tissue cannot be denied. Since 1934, when the theorem of the probable relationship between testicular hormones and carcinoma of the prostate was discussed by this essayist before the Southwestern Branch of the American Urological Association, in St. Louis, extensive correlative clinical, pathological, and biochemical studies have led to the evolution of a specific, though limited, therapeutic technic.

The investigative work of Kutscher and Wolbergs (2) established that the normal prostate tissue is extremely rich in the enzyme, "acid" phosphatase. The Gutmans (3) found acid phosphatase in primary tumors of the prostate and also in metastases at various sites. Determination of the serum acid phosphatase level, then, is a valuable aid in the diagnosis of bone lesions secondary to carcinoma of the prostate. Whenever the acid phosphatase level has been found to be appreciably increased, metastases have invariably been present. They may, however, occur without a rise in the acid phosphatase level. Thus there are false negative but no false positive reactions.

A high serum "alkaline" phosphatase level is of value in differentiating Paget's disease of the bone from bone metastases arising from carcinoma of the prostate. The alkaline phosphatase level is high, also, in biliary obstruction, generalized osteoporosis, hyperthyroidism, and active rickets.

The activity of the male hormone influences the growth of adult prostatic epithelial cells which characterizes prostatic carcinoma. This activity may be measured by the serum acid phosphatase determination.

Most malignant prostate tumors are adenocarcinomas and consequently relatively radioresistant. It is noteworthy, nevertheless, that they are decidedly more radiosensitive than the same type of tumor in the digestive tract. A comparative histologic study of tumor tissue in several instances, before and after high-voltage irradiation, shows a varying degree of cellular damage. Not infrequently one observes complete destruction of the nucleus, with only the cell walls remaining visible. A varying degree of pyknosis, with a clear pale-staining substance distending the cytoplasm, is seen in certain instances, while again the cytoplasm is granular, with marked karyokinesis. In no instance is there such extensive cellular damage that one cannot find scattered cells retaining their viable staining characteristics.

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[1] Presented at the Joint Meeting of the American Roentgen Ray Society and the Radiological Society of North America, Chicago, Ill., Sept. 24–29, 1944.

It is quite the universal concept to limit the origin of carcinoma to the posterior lobe. This idea should be dissipated; cancer may, and does, originate in any portion of the prostate or its lobules. This fact is most important in judging the clinical index for therapeutic purposes. The fixed indurated nodule palpated in the posterior lobe in a patient under sixty years of age is more actively malignant than the large nodular tumor palpable rectally in a patient past sixty years.

In 1932, a study correlating the pathological data and clinical observations in 501 cases established a satisfactory clinical index for therapeutic purposes. *Group A*, or the least malignant group, comprising 62 per cent of the cases, is characterized by an age factor of 65 or over, with 200 c.c. or more of urine, the tumor developing in an already established benign hypertrophy and presenting the histologic characteristics of adenocarcinoma with mature cells and definite alveolar structure. *Group B*, intermediate in malignancy, accounts for 26 per cent of the cases; the patients are between 55 and 65 years of age, with symptoms of ten to twenty months' duration. They frequently complain of pain but give no evidence of metastasis. Examination reveals a small, firm, irregular tumor. Histologic study shows anaplasia, with rapid disappearance of the adenomatous characteristics. *Group C*, the most malignant group, comprises the remaining 12 per cent of cases. The patients are under 55 years of age, with little or no residual urine, with pain and demonstrable metastases, and with symptoms usually of less than a year's duration. Rectal examination reveals a rather small, diffusely indurated prostate, not characteristically diagnostic, with a histologic picture of small round cells and anaplasia. While this classification cannot always be arbitrarily applied, it helps greatly, nevertheless, in the selection of therapy and establishing prognosis.

In a report (4) before the American Urological Association in 1941, dissipation of the androgenic hormone by direct testicular irradiation in addition to regional irradiation was advocated in the treatment of carcinoma of the prostate. A study of 11 cases was presented, all of which had been treated by prostatic resection and regional irradiation, with adjunct irradiation directly to the testicles. When the report was rendered, 8 of the 11 patients were alive, the longest survival being seven and the shortest three years. Five of the surviving patients had been examined during the year of the report. Rectal examination in almost every instance presented minimal findings which would lead the examiner to conjecture a diagnosis of carcinoma of the prostate. The prostatic bed was usually smooth, resilient, and free of nodules. From the comparative study made in that report, it was concluded that the addition of planned testicular irradiation definitely enhanced the survival chances of the patient. It is known that at least 3 patients from the series reported in 1941 are still living.

This presentation is concerned with further clinical experiences as the result of therapeutic application of x-rays. Huggins (5), in a discussion of the effect of irradiation of the testes in advanced prostatic cancer, presents the clinical course in two cases in which the testicles were not subjected to direct planned irradiation but were dependent upon "back-scatter" from regional irradiation. Indeed, in one case the testes were protected in the usual way with lead rubber but undoubtedly received back-scattering of radiation. Six months later this patient was given regional irradiation without protection of the testes. Huggins says: "The testes in each case presented similar cytologic characteristics, namely, profound atrophy of the germinal epithelium with preservation of Sertoli cells and apparent or real hyperplasia of the Leydig cells." He concludes: "It is thus apparent that roentgen ray irradiation, in the amounts stated, is ineffective in destroying the secretory function of the testes and is inadequate as a therapeutic agent in prostatic cancer in man."

It is unfortunate that so good a research worker as Huggins should publish such an

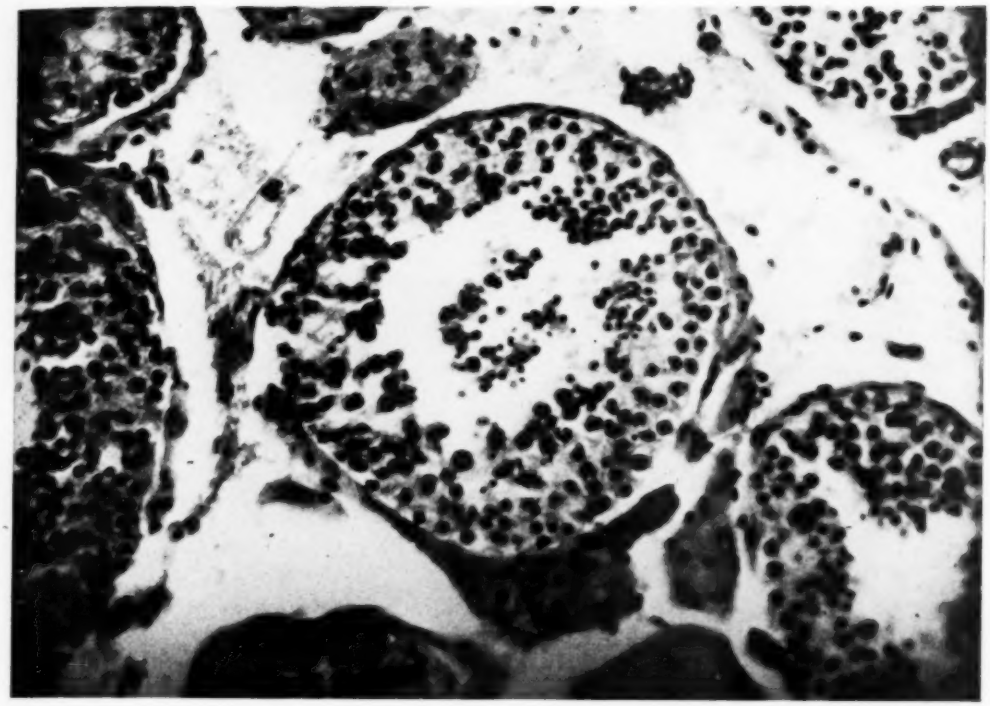


Fig. 1. Histology of the normal testicle showing seminiferous tubules with spermatogenic cellular elements, the loose interstitial meshwork of fibrous reticulum representing the so-called interstitial or Leydig cells.

inaccurate and inadequate report. Without a parallel series of roentgen and surgical castration cases, he is not in a position to pronounce a negative dictum relative to the effects of planned testicular irradiation. That the effect on the testicular elements, in the dosage used, is profound is testified to by the accompanying illustrations. It is not within my province, as a urologist, to discuss before a meeting of roentgenologists the technical factors involved in testicular irradiation. A sample report reads as follows: "In way of summary, this patient began his irradiation therapy May 22, 1942, at which time he was given 1,800 r direct irradiation to the testicles, divided into daily doses of 300 r. The quality of beam used in this therapy is 200 kv.p., 1.5 mm. copper + 1 mm. aluminum, half-value layer 0.9 mm. copper. Beginning May 29, 1942, this patient received fractionated irradiation about the pelvis using a beam with half-value layer of 3.5 mm. copper, kv.p. 400. He received a total of 2,000 r (in air) to each of four pelvic ports, which gives a depth dose, of about 5,500 tissue roentgens to the mid pelvis."

It is, however, incumbent that the clinical picture be discussed. As a prelude to any treatment, a biopsy study is mandatory to determine the type and grade of the tumor, and a roentgenologic and phosphatase-level survey is made for metastases. An attempt is made to classify the case in accordance with the clinico-pathological criteria aforementioned for determining upon intensity of treatment and for purposes of prognosis. As a rule, I find that the case dovetails into this classification quite well.

During the two-year period ending in May 1943, 27 cases of carcinoma of the prostate were seen, 12 of which were treated by resection with regional and testicular irradiation, 8 by resection, irradia-

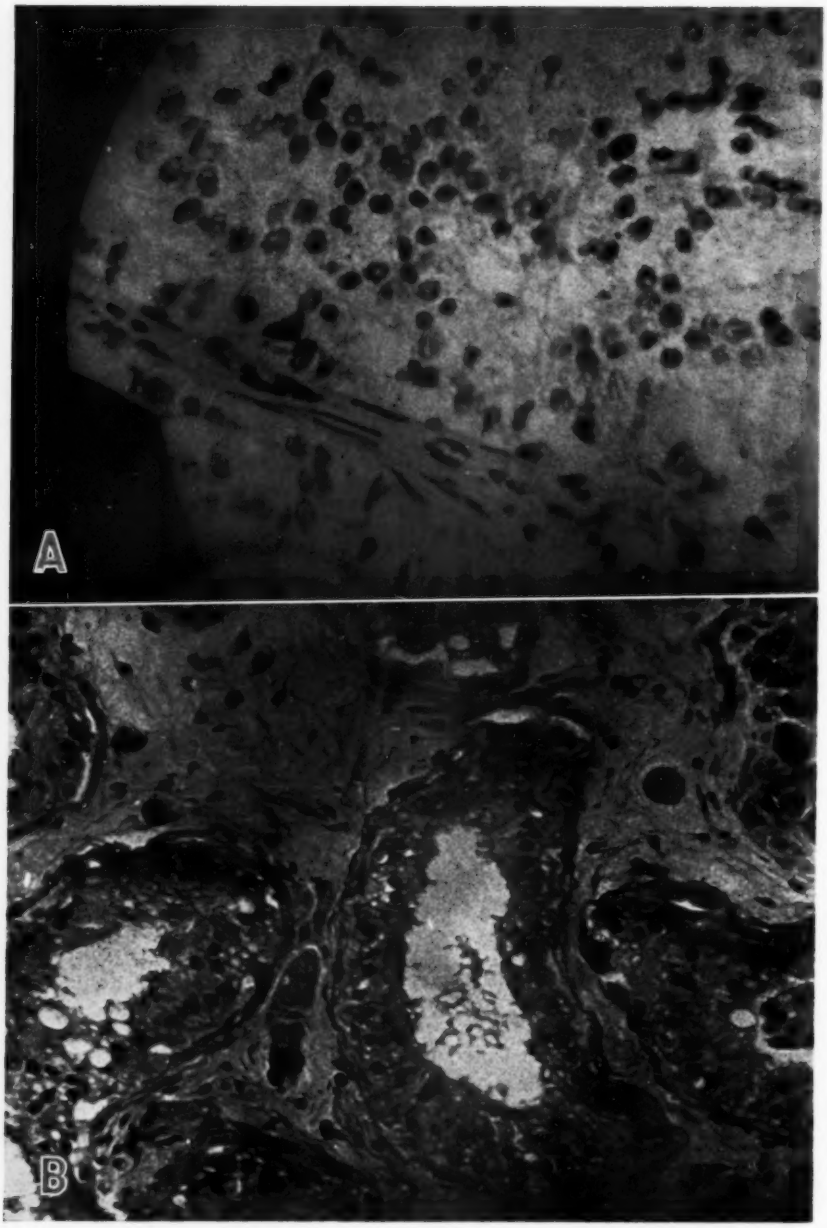


Fig. 2. A. Histology of Grade III adenocarcinoma of prostate following resection and before irradiation of testicles.

B. Histologic appearance of testicle in the same case immediately after 1,200 r to testicles and 47 days after 1,800 r to the pelvic region. Note swelling of interstitial fibrous reticulum with apparent hypertrophy of Leydig cells and marked degeneration of spermatogenic cellular structures. See also Fig. 2, C and D.

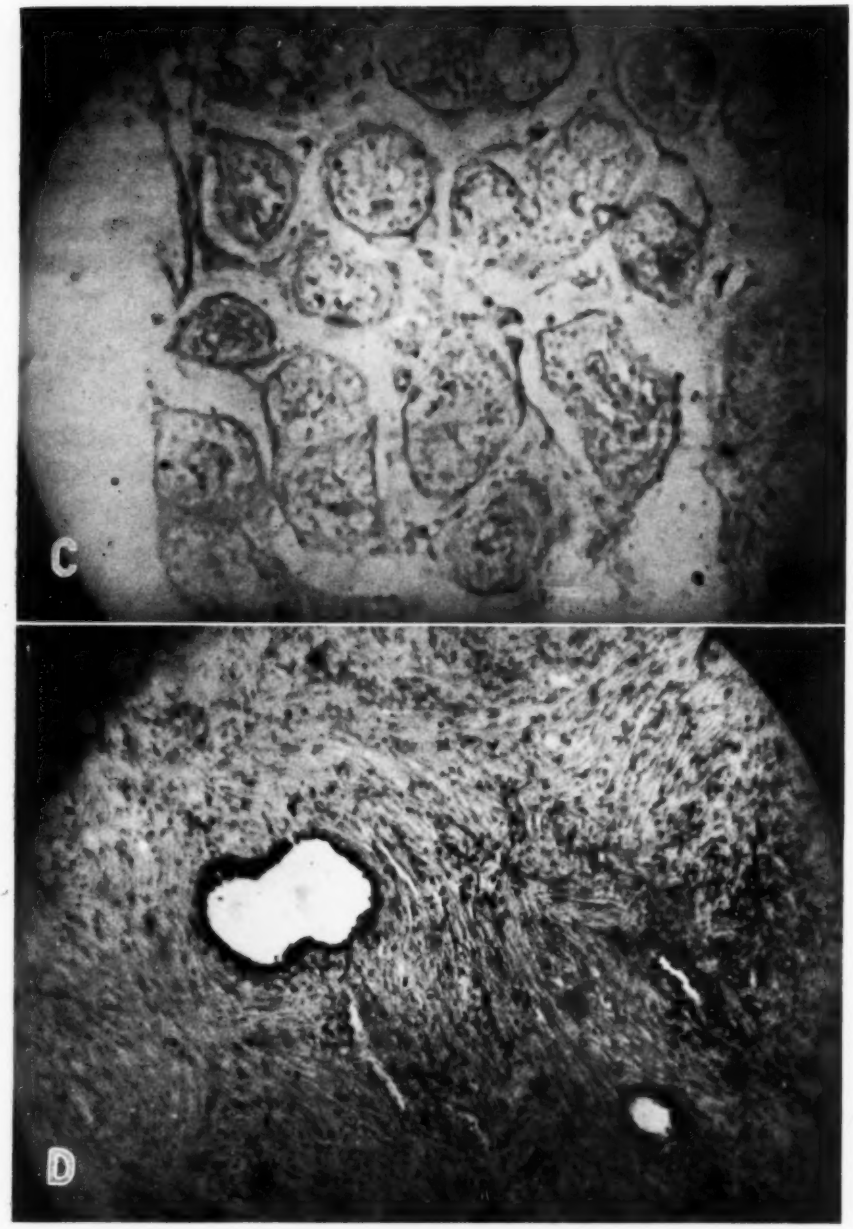
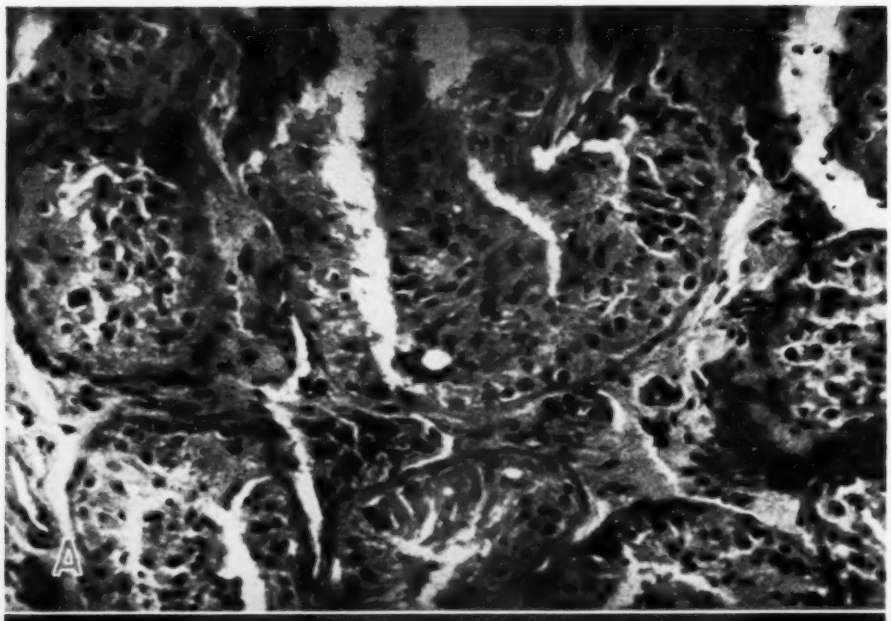


Fig. 2. C. Section of testicle (from case shown in Fig. 2, A and B) one year after irradiation, showing marked degenerative change in spermatogenic cellular elements with complete destruction and dissipation of Leydig cells. (Biopsy taken by courtesy of Dr. Roger Barnes and section made by pathologist in White Memorial Hospital, Los Angeles.)

D. Section of prostate (from same case) taken one year after original biopsy showing carcinoma and one year after 1,500 r testicular and 1,800 r regional irradiation. This study reveals no histologic evidence of carcinoma of the prostate. (Biopsy taken and study made in White Memorial Hospital, Los Angeles.)



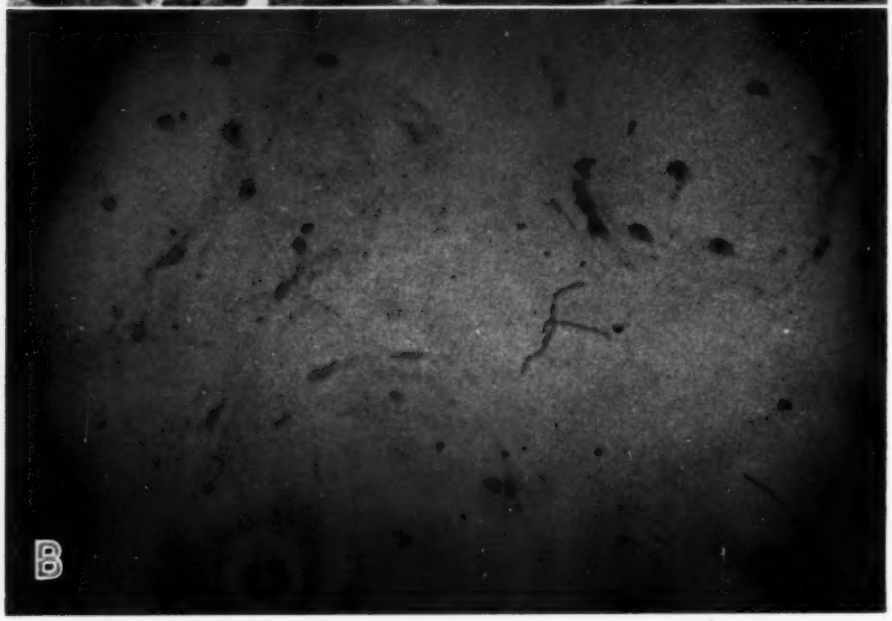


Fig. 3. A. Section of right testicle 24 days after direct irradiation with 1,500 r, showing marked swelling of the spermatogenic cells, destruction of the basement membrane, increase in the interstitial reticulum, and swelling of the Leydig cells.

B. Section of same testicle 18 months after direct irradiation with 1,500 r, showing complete destruction of all elements, especially interstitial. See also Fig. 3, C.

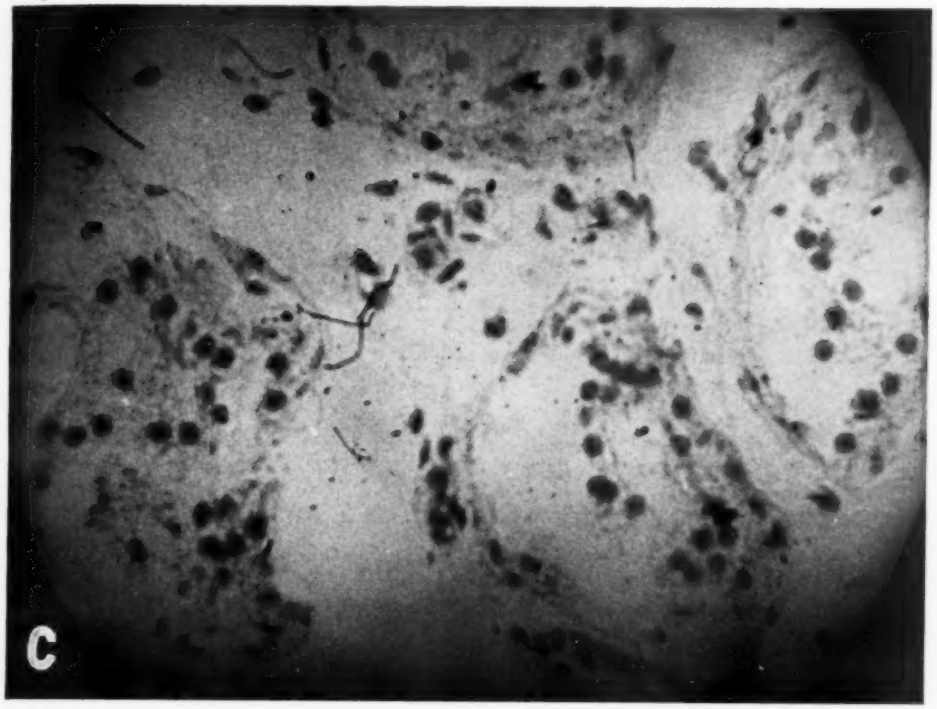


Fig. 3. C. Section of left testicle (same case as Fig. 3, A and B) 18 months after irradiation of the pelvic region, the testicle receiving back-scatter only. The destruction is not nearly so evident as in the right testicle, which received direct irradiation. This left testicle was "leaded off" when direct irradiation was given to the right testicle.

tion, and estrogen therapy, and 7 by orchiectomy.

Of the 27 patients, 5 are dead at the date of this report. Two of these were subjected to primary surgical castration, one on my service and one elsewhere. Both manifested primary improvement in their osseous and remote metastases, with secondary reactivation. All forms of treatment were without avail, and the patients died at nine and thirteen months, respectively. One patient was admitted with a large, soft rectal and intravesical intrusion. The diagnosis was hypertrophied prostate, and a prostatectomy was performed. The pathologist reported most of the tissue to be benign adenoma but with several sections showing Grade IV adenocarcinoma. Regional and testicular irradiation was promptly instituted but rapid osseous and pulmonary metastases ensued. The phosphatase level in this case was 2.8 units (K.A.) when taken promptly upon report of carcinoma by the pathologist. Nevertheless, it is felt that metastases were well advanced on admission. The phosphatase level rose progressively to 14.2 units (K.A.) in keeping with the spreading metastases. Two months after irradiation, an orchiectomy was done but did not change the course of events. The patient died eleven months following prostatectomy, of generalized metastases. The fourth death occurred seventeen months after resection followed by partial regional irradiation only. Because of a severe systemic reaction the patient, a diabetic, refused further treatment. Over the several months following resection, the phosphatase level ascended to 8.8 units, with metastases and pathological fracture of the right femur. Death was apparently due to carcinoma.

The fifth death was that of a physician who was seen with a well advanced but non-metastasizing carcinoma. He wanted an orchiectomy but his wife refused orchiectomy in favor of testicular irradiation. Regional and testicular irradiation and estrogen therapy were given, producing a remarkable stabilization. The phosphatase level was at all times within normal range, but death occurred in twelve months from a cerebral hemorrhage.

In surgical castration there can be no question but that the testicular carcinogenic factor is removed with the testicle. But to my mind, the gates are thus ostensibly closed to proper search by the pathologist and biochemist for that unknown factor—shall we call it factor X?—in the biochemical economy which might with more certainty answer the question of endocrine relationship to carcinoma. Estrogen therapy is probably fundamentally the most scientific approach to this subject. But surgical castration and estrogen therapy are in themselves subjects for monographs.

All the patients in this series had proved carcinomas, graded by biopsy. In all cases phosphatase level determinations were made. Of the 12 patients treated by resection with regional and testicular irradiation, 7 had well developed osseous and remote metastases when first seen, and 3 of these are among the dead discussed above. In 5 of the 7 showing metastases when admitted, the disease is reasonably well stabilized. At least, the metastases are not progressive, although in 2 cases a high phosphatase level has been maintained from the time the patient was first seen. All 5 men are normally active for their age and on rectal examination the prostates show a firm smooth bed which would be hard to diagnose clinically as carcinoma. The remaining 5 of this group of 12 patients are showing satisfactory stabilization. None of these showed metastases, and none had a phosphatase level considered above normal (4 units K.A.). There are 3 grade II and 2 grade I tumors in this group.

Of the 7 patients treated by orchiectomy, 5 are still living, the longest survival period being twenty-eight months and the shortest sixteen months. Three had metastases when originally seen. In all cases resection was done (if only for biopsy purposes). All showed prompt symptomatic relief and physical improvement following castration; the 2 deaths were due to reactivated metastases. Of the 5 surviving patients, only 2 show good stabilization. Each at varying periods after castration had recurrent symptoms suggestive of reactivated carcinoma, and as this occurred, estrogen therapy was instituted. It is felt that the best estrogenic response is obtained with the true hormone, ethinyl estradiol (Estinyl-Schering). Reactivation, on the average, was earlier and more intense than in the irradiated cases. Two cases responded well to estrogen intake, whereas in 3 the response was indifferent. Only 2 of the patients undergoing orchiectomy are as stable in physique and well-being as are the similar ones treated by resection and irradiation.

The profoundest stabilization has occurred among those who received resection, testicular and regional irradiation, and adjunct estrogen therapy coincident with the x-ray treatments. In this group there were 3 grade IV, 2 grade II, and 1 grade III tumors. There has been one death, from cerebral hemorrhage. The irradiation response was decidedly more acute in each case, and stabilization has been much more definitive over the months than after any other procedure. All cases are now being treated with this combination of therapy. The reasons for this profound response are entirely speculative. It is assumed that the depressant action of the estrogen is enhanced because of the vitiating effect of the x-ray on both the gonadal and extragonadal depots of androgen production. Certainly the estrogen response is more noticeably effective in the case being irradiated than the case which is not.

SUMMARY

1. Carcinoma of the prostate constitutes about 14 per cent of all prostatic tumors.

2. The development of carcinoma of the prostate is seemingly related to the gonadal and extragonadal depots of androgen production.

3. Surgical castration relieves only the gonadal depots of hormonal production.

4. Adequate testicular and regional irradiation definitely dissipates hormonal production.

5. The female hormone (estrogen) depresses androgenic activity.

6. The most effective stabilizing treatment in carcinoma of the prostate is a combination of regional and testicular irradiation with an estrogen.

7. Thorough systemic diagnostic study for metastases, with biopsy and grading of the tumor, must be instituted in each case before treatment.

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DISCUSSION

Edward W. Rowe, M.D. (Lincoln, Nebraska): It is a pleasure to say a word for the enthusiasm and the deep interest in this radiological problem by a fellow townsman, Dr. Munger. As for myself, I think my technic is a good deal like that which he describes. In the beginning, we tried to treat carcinoma of the prostate by irradiating the prostate and the surrounding parts. We lost sight of the testicles. Then the movement was toward treating the testicles and ignoring the prostate. Dr. Munger has made the statement that both must be thoroughly irradiated.

For my part, I keep track accurately of the surface dosage and try to estimate the depth dose. In so doing I think we have a fairly accurate idea of the total radiation received.

When it comes to treating the testicle, I believe that we should not depend upon back-scatter, as we did formerly, but that we should protect the testicle except when treating it specifically, in which case we should know just how large a dose it is receiving.

Roentgen Study of the Ankle in Severe Sprains and Dislocations[1]

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Philadelphia, Penna.

THERE HAS MORE recently been an increasing tendency toward the use of the x-rays in clinical medicine to demonstrate not only the anatomical structure and pathological lesions of a part but also its physiology and any disturbances thereof. This is well illustrated in roentgen studies of the urinary and digestive tracts. The study of the skeletal system has not kept pace with that of other systems in this respect and, even today, is for the most part on a purely anatomical basis.

In examination of the ankle, roentgenograms are obtained, as a rule, in the anteroposterior and lateral positions. If no bony injury or abnormality is demonstrable, the report usually reads: "Nothing abnormal is seen, but this examination does not exclude injury to the soft parts." In other words, our examination fails to record the presence of a soft-tissue injury. This was brought forcibly to our attention by the following case:

CASE REPORT

R. M. U., a white male, 53 years of age, was admitted to the service of Dr. Paul C. Colonna at the Hospital of the University of Pennsylvania on Sept. 19, 1943, having been thrown from a horse the day before, at which time his right foot was forced into inversion and adduction. At the time of admission the ankle was moderately swollen and extremely tender around the external malleolus and very painful on motion. There was some ecchymosis around the lateral aspect.

Anteroposterior and lateral roentgenograms showed only two small smooth fragments of bone lying in the soft tissues below the internal malleolus, which were interpreted as representing an old fracture of that part (Fig. 1).

Because the symptoms were suggestive of more than the usual sprain, the surgeons in charge of the case requested anteroposterior roentgenograms with

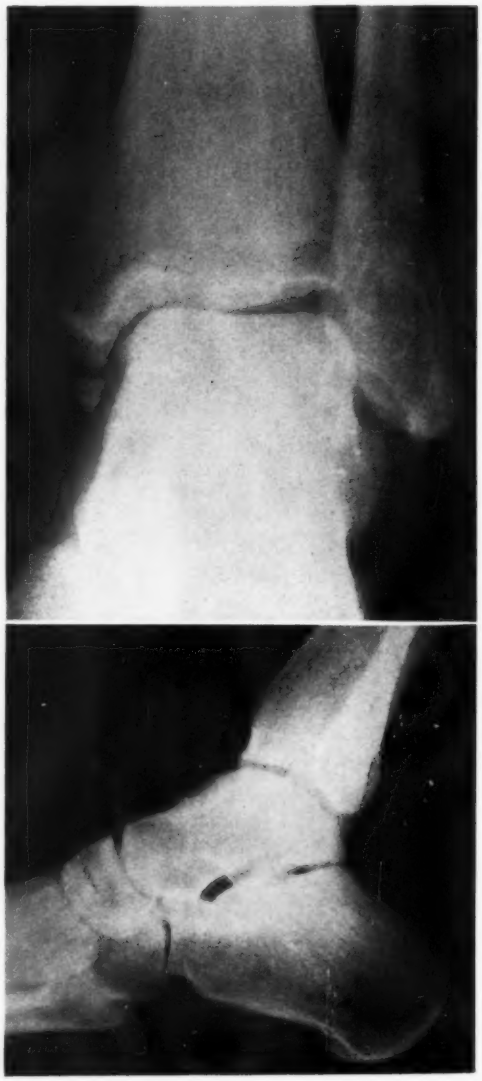

Fig. 1. Ankle at the time of injury. The anteroposterior view shows only two small fragments of the medial malleolus, which were thought to represent an old injury. The lateral view shows nothing abnormal.

[1] From the Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, Penna. Accepted for publication in November 1944.

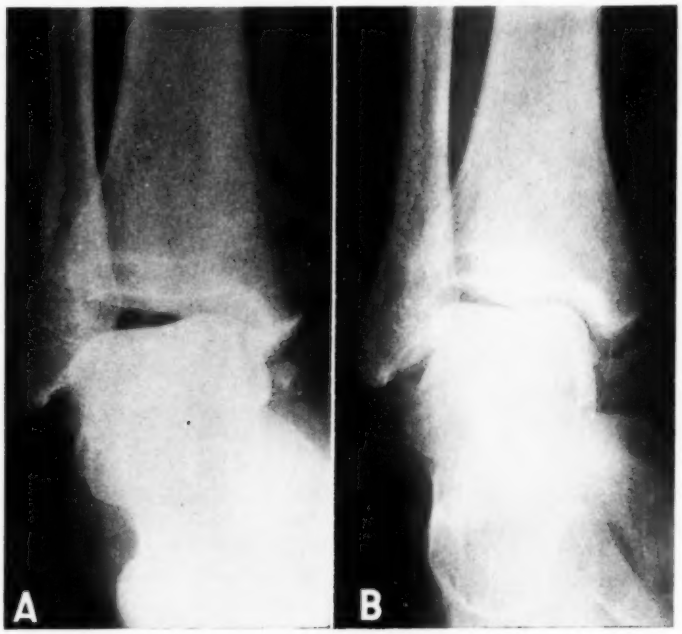

Fig. 2. A. Anteroposterior view of the foot at the time of injury, in forced inversion, showing a widening of the tibio-astragalar joint, which is the sign of tear of the lateral ligaments.
B. The foot held in forced inversion after immobilization for four weeks. There is now no widening of the tibio-astragalar joint.

the foot held in forced inversion and then in forced eversion. The study made in forced inversion showed that the talus had tilted in the ankle mortise and this had produced an increase in the joint space between the talus and the tibia (Fig. 2, A). It was felt that this indicated excessive relaxation, stretching, or tearing of the ligaments of the ankle; a report was made of a probable excess of mobility of the talus upon the tibia, and the foot was immobilized in plaster for four weeks. At the end of that time the two small fragments at the tip of the medial malleolus were unchanged, but there was no evidence of spread of the tibio-astragalar joint space on forced inversion (Fig. 2, B).

DISCUSSION

Realizing from this case how little we knew of the normal ankle when it was subjected to strain, we obtained roentgenograms of six normal ankles in inversion and eversion, and in none of these found any change in either the joint space between the talus and the tibia, or in the relationship of the tibia and fibula to each other (Fig. 3, A, B, C).

The ankle is a ginglymus or hinge joint which is made up of the lower end of the tibia and the malleoli of the tibia and fibula. These bones, with the transverse ligament, form a mortise for the upper convex surface and lateral facets of the talus. The ligaments of the joint (Fig. 4) are as follows: the surrounding articular capsule; the deltoid or internal lateral ligament; the anterior talofibular ligament; the posterior talofibular ligament; the calcaneofibular ligament. These last three are known also as the anterior, middle, and posterior fasciculi of the external lateral ligament (2).

According to Watson-Jones (3), an injury causing rupture or severe stretching of the external lateral ligament would produce a picture such as was seen in the above case, and he considers this injury a partial dislocation at the ankle joint. He recommends anteroposterior roentgenograms in forced inversion and eversion for its diagnosis (3). Elmslie also discusses

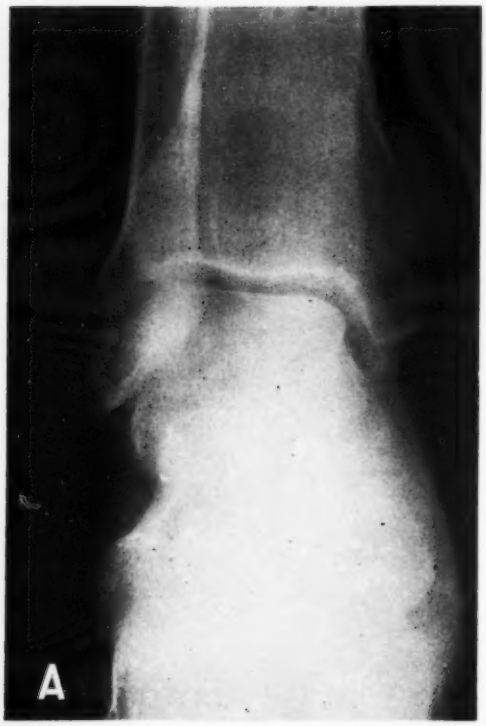

Fig. 3. A. The normal ankle.

this syndrome (1). He attributes it to rupture or stretching involving only the anterior and middle fasciculi of the external lateral ligament and says that this is the injury which occurs when the foot is held in plantar flexion and inverted. This allows the talus to tilt in the mortise. In the usual sprained ankle the foot is held in dorsiflexion and only the anterior ligament is injured. If this ligament fails to heal, no instability of the joint occurs, but if the two fasciculi are torn, and fail to heal, as is their tendency, an unstable joint results. Elmslie believes that in an injury of this sort the ruptured ligaments will have to be sutured, but the cases with which he was dealing were old and chronic. For fresh injuries of this type, Watson-Jones recommends immobilization in plaster for four to six weeks (3).

In studying the ankle following an injury, we believe that routine anteroposterior and lateral views should be made.

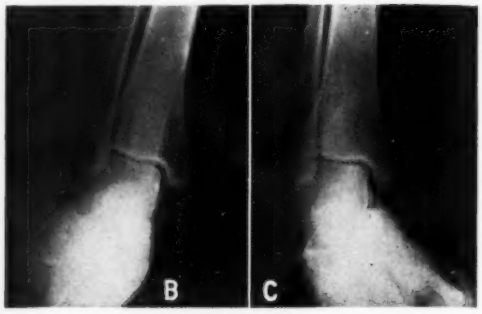

Fig. 3. B and C. The normal ankle in forced eversion (B) and in forced inversion (C). Note that there is no widening of the tibio-astragalar joint.

If these fail to show evidence of bony injury and the symptoms are suggestive of a fracture, dislocation (3), or subluxation (1) at the ankle joint, then roentgenograms should be made with the foot held in forced inversion and eversion and forced flexion and extension. The normal ankle in the anteroposterior view and in inversion and eversion is shown in Figure 3. Figure 5 shows the lateral view in the midposition, in flexion, and in extension.

This type of examination is indicated in patients with a recurrent ankle sprain without severe pain, in those with a history of instability of the ankle, in those with abnormal motility of the ankle joint with a hollow instead of a swelling anterior to the external malleolus (1), and as pointed out above, in all patients with clinical symptoms suggesting more than a simple sprain in whom no evidence of bony injury can be found. We also feel that any severe sprain that is to be treated by procaine injection should have this type of examination because of the possibilities of an unstable ankle if the external lateral ligaments are torn and not treated by immobilization as recommended by authorities on the subject (1, 3).

Before carrying out the examination, the permission of the referring doctor must be obtained, and all dressings and tape on the ankle must be removed. It is occasionally possible to demonstrate such an injury clinically and in those cases it is probable that the referring physician may feel that further examination is unnecessary. On

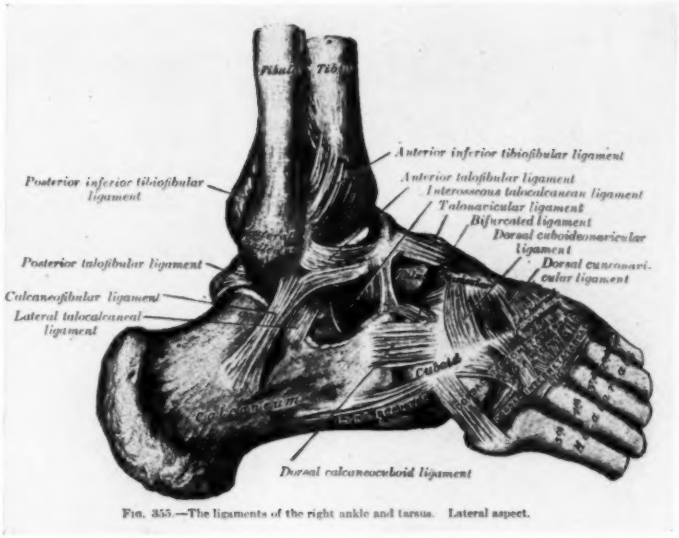

FIG. 355.—The ligaments of the right ankle and tarsus. Lateral aspect.

Fig. 4. Lateral aspect of the ankle, showing the ligaments. Those involved in this type of injury are the anterior talofibular, the posterior talofibular, and the calcaneofibular. (Reproduced from Gray's Anatomy by permission of Lea & Febiger.)

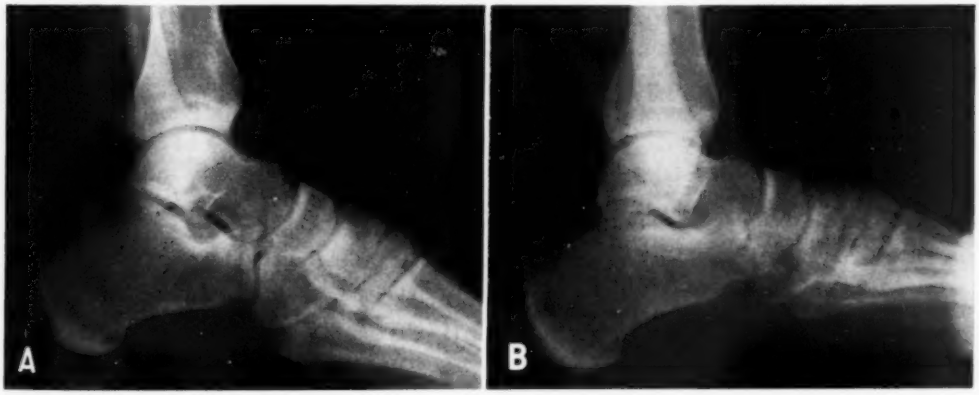

Fig. 5. A and B. The normal ankle. A. Lateral view. B. Lateral view in forced flexion. See also Fig. 5, C.

the other hand, the roentgenogram constitutes a permanent record, which may be of inestimable value in compensation cases as well as those of general practice.

During the examination the foot must be held by an assistant, preferably a member of the surgical staff, but care should be taken that this assistant is not subject to excessive radiation exposure on repeated examinations. The manipulation of the joint is less painful for the patient if 5 or 10 c.c. of procaine is injected around the point of maximum tenderness, although this is not essential. Here again the permission of the referring doctor should be obtained if anesthesia is to be employed. The examination to determine mobility of the joint should be reserved as a supplementary procedure and not employed as a routine.

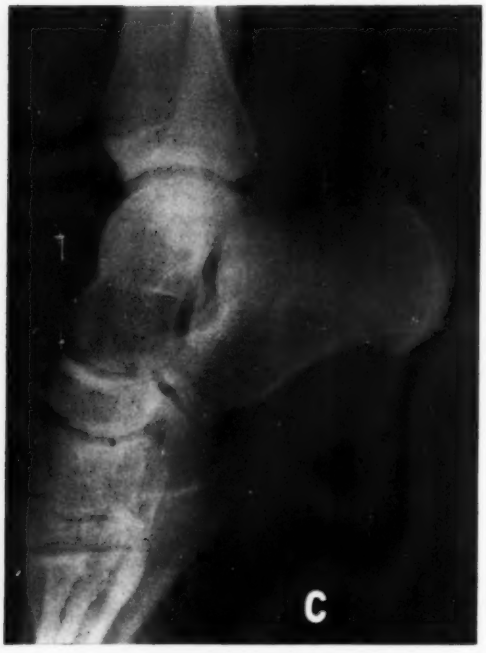

Fig. 5. C. Normal ankle in forced extension.

SUMMARY

A type of dislocation of the ankle is described in which the usual anteroposterior and lateral roentgenograms appear normal. It is due to rupture or stretching of the external lateral ligaments of the ankle joint and is demonstrable in anteroposterior roentgenograms of the ankle in forced inversion, showing widening of the tibioastragalar joint space. Roentgenograms of normal ankles in inversion, eversion, flexion, and extension are shown for comparison. Indications for this type of examination are discussed.

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Osteogenic Sarcoma of the Skull[1]

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PRIMARY osteogenic sarcoma of the skull is an exceedingly rare entity. Camp, in a wide experience with skull roentgenography extending over approximately twenty-five years, recollects seeing only four or five examples (1). Examination of several standard textbooks on pathology and roentgenology discloses no reported cases.

Osteogenic sarcoma of the skull secondary to long standing osteodystrophia fibrosa hyperostotica (Paget's disease) is a not uncommon entity. It is estimated that in anywhere from 2 to 10 per cent of patients with Paget's disease of the skull such a condition eventually develops. This type of malignant growth is inherently secondary rather than primary and is most likely to occur in the age period when osteogenic sarcoma is a rarity. We have seen 5 cases of osteogenic sarcoma complicating Paget's disease of the skull, all in persons over fifty-five years of age, during a ten-year period ending in 1942 (chiefly on the Stanford University X-ray Service at the San Francisco City Hospital).

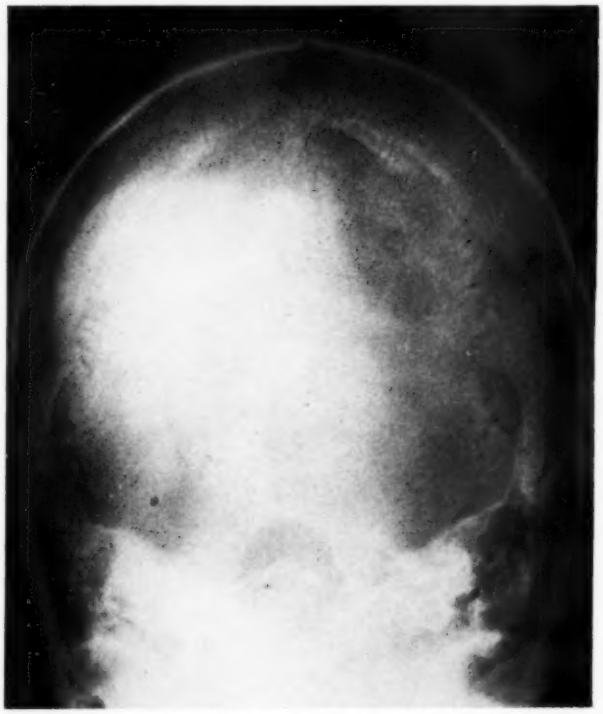

Fig. 1. Anteroposterior (occipital) projection of the skull showing irregular increase in density of the occipital bone, involving an area about 8 cm. in diameter.

Primary osteogenic sarcoma of bone is essentially a disease of the young, its incidence reaching a peak at fifteen years of age. It occurs twice as commonly in males as in females, and over 50 per cent of cases arise in one of the bones of the

[1] Accepted for publication in October 1944. The opinions expressed herein are those of the writer and are not to be construed as official or reflecting the views of the Navy Department.

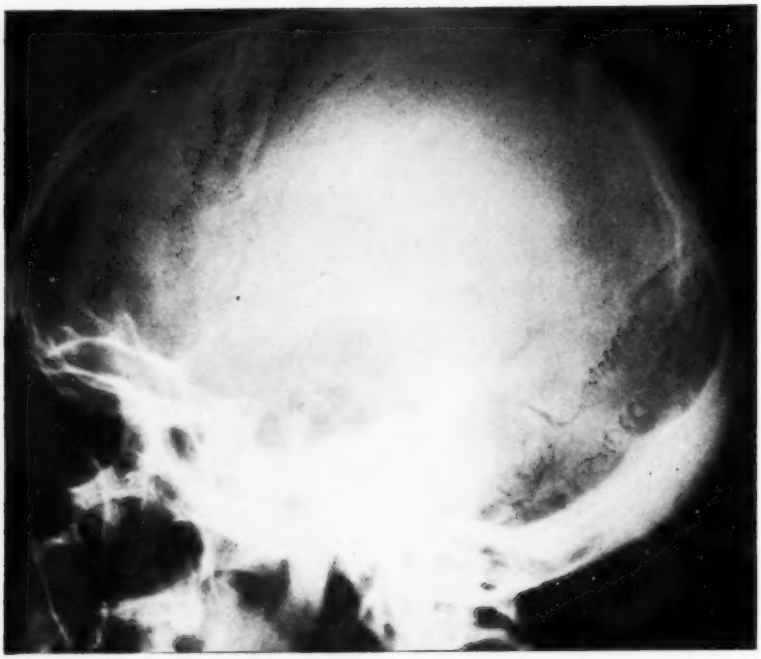

Fig. 2. Right lateral projection of the skull. The outer table alone appears to be involved.

Fig. 3. Soft-tissue lateral projection of the tumor, showing spicule formation and calcification. Microscopic diagnosis: osteogenic sarcoma.

lower extremity (2). Less than 1.0 per cent of cases develop in the skull bones. In view of this incidence, the following case is being reported.

A seaman aged 17 reported to sickbay for examination of a lump on the back of his neck, at the base of his skull. He stated that the lump had grown during the preceding two months, was slightly painful, and caused some limitation of cranial movements. Its most prominent portion lay slightly to the right of the mid-line and it felt about the size of a ping-pong ball. Except for the mass, the patient felt and appeared quite well. The surgeon who saw him made a tentative diagnosis of osteochondroma and removed the mass on Feb. 2, 1944, at a Mid-Pacific Base Hospital. The biopsy report is not available.

Recovery was prompt, and the patient returned to duty. After about eight weeks, the lump recurred and was slightly more painful than before. The patient was sent back to a Naval Hospital on the Pacific Coast, where he reported at the end of April. He was a well built and apparently healthy young male, with no complaints beyond those above described. The mass had grown to about 8 cm. in diameter and was hard and fixed. The scar from the previous operation appeared healthy. X-ray examination of the lungs was negative. The skull showed extensive thickening of the outer table of the occipital bone, chiefly to the right of the mid-line, with considerable spiculation and a small amount of irregular calcification in the tumor (see Figs. 1–3). In many respects the x-ray appearance resembled that of an endothelioma, but the bone formation was, of course, on the "wrong" side of the calvarium for such an entity. Stereoscopic lateral, oblique, and tangential projections all failed to disclose any evidence of involvement of the inner table. The roentgen diagnosis was tumor of the occipital bone, malignant, presumably some type of osteogenic sarcoma.

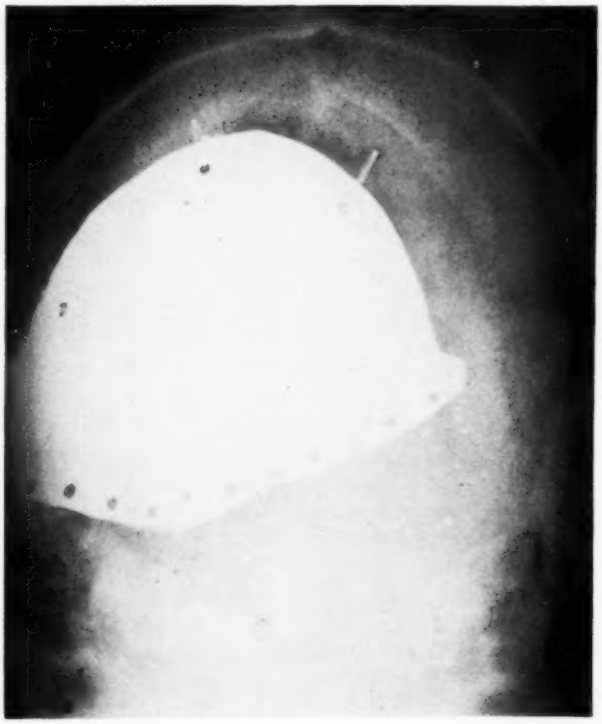

Fig. 4. Occipital projection, postoperative, showing tantalum plate *in situ*.

On May 1, 1944, Lt. Comdr. F. K. Bradford performed a radical operation, resecting most of the occipital bone. Grossly the tumor appeared to be malignant and to have invaded the muscles of the neck. The surgeon removed as much of these muscles and of the ligamentum nuchae as he dared and replaced the bone with a molded tantalum plate. The plate was attached securely to the skull, and the remaining posterior cervical muscles were then attached to the plate (Figs. 4 and 5).

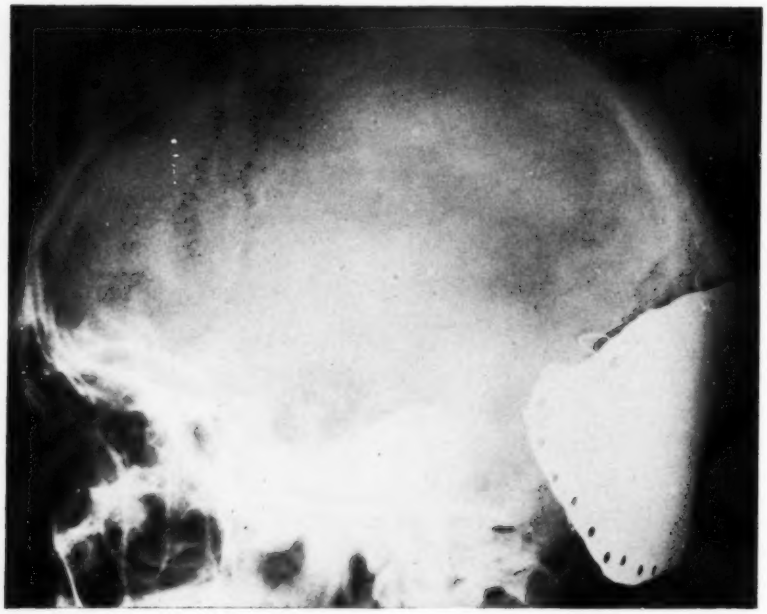

Fig. 5. Lateral projection, postoperative, showing tantalum plate *in situ*

The pathological report (by Lt. Comdr. L. H. Dyke) was as follows: The gross specimen consists of a strip of scarred skin, some subcutaneous tissue, and numerous masses of bone and muscle, all measuring 12 × 12 × 5 cm. There is a neoplastic mass 8 cm. in diameter, which has been completely excised; this contains numerous spicules of bone. Portion of the occipital bone shows infiltration of the outer table by neoplasm, but no gross infiltration of the inner table. Microscopically, the tumor is composed of pleomorphic, spindle-shaped cells, rather variable in size and shape, with fairly frequent mitotic figures; these cells infiltrate a dense supporting stroma between masses of bone. There are some areas of new bone formation and some of metaplasia, forming small islands of cartilage. Diagnosis: sarcoma, osteoblastic and osteogenic.

Immediately after the preoperative roentgen examination, a course of roentgen irradiation had been started; this was continued following operation. The patient was treated in the prone position, through one large posterior portal, 15 × 15 cm., covering the back of the skull and upper posterior neck. He was given 2,500 r (air) between April 28 and May 24, 1944, with a 200-kv. beam, half-value layer 1 mm. Cu.

Young and unusually sanguine, the patient made a rapid recovery and was discharged one month after conclusion of the roentgen irradiation course. At the time of this report, he is still clinically well, but we regard the prognosis as quite hopeless.

SUMMARY

A case of osteogenic sarcoma of the occipital bone in a male aged seventeen years is reported. The tumor was subjected to radical excision and the tumor site to fairly heavy roentgen irradiation. The rarity of tumors of this type is emphasized.

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Relationship Between Morphology and X-Ray Effects in Implants of Mouse Sarcoma 180 Irradiated with 5,000 and 60,000 Roentgens (in Air)[1]

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THE EXPERIMENT to be described in this paper deals with the morphology of implants of mouse sarcoma 180 previously irradiated with 5,000 r (in air), as compared with that of implants irradiated with 60,000 r (in air) and unirradiated controls, as they appeared during ten successive days following implantation into 100 per cent susceptible mice.

This is an extension of previous investigations in which it was demonstrated (*a*) that a dose of 60,000 r, measured in air, was required to prevent the proliferation of explants of mouse sarcoma 180 in a culture medium *in vitro* (1); (*b*) that a dose of 5,000 r was sufficient to prevent implants from producing a detectable tumor *in vivo* in a strain in which control implants were 100 per cent successful (2); (*c*) that animals implanted with tumor fragments irradiated with 5,000 r became resistant to subsequent implants of the same type of tumor, while those animals implanted with tumor fragments irradiated with 60,000 r did not (3).

Several authors (4–9) have investigated the reaction of an immune host to viable tumor implants, but there has apparently been no cytological study of tumor implants inducing resistance in 100 per cent susceptible hosts.

EXPERIMENTAL PROCEDURE

The same strain of mice (C.F.X. strain from Carworth Farms) was used here as in the previous experiments (1–3), and the experimental procedure was similar. An eight-day-old tumor was removed from the host under aseptic precautions. In order to secure actively growing cells and to avoid necrosis, only portions from the periphery of the tumor were taken for implants. With a cataract knife, fragments were cut, ranging from 1 to 2 mg. in weight, from 1.2 to 1.5 mm. in length, and from 1.4 to 0.9 mm. in thickness. These fragments were divided into three portions. Each was placed on a No. 1 coverslip, which had been previously attached to a square mica sheet, covered with a Maximow slide, and sealed with paraffin. To avoid evaporation, a fragment of moist filter paper was placed in the concavity of the Maximow slide. One portion of the tumor fragments was then irradiated with 5,000 r, measured in air without backscatter, and another with 60,000 r. The third portion, which was not irradiated, was used for a control. The physical factors were as follows: 200 kv., 20 ma., 0.5 mm. Cu + 1.0 mm. Al, half-value layer equivalent to 0.85 mm. Cu, focal tissue-target distance 12.5 cm., with a dosage rate of 612 r per min. measured in air. Immediately after irradiation, the tumor fragments were implanted into animals by means of a trocar. The chosen site for implantation was about the middle of the abdomen, between the groin and the axilla. This site was found by Russell (4) to be the most suitable, for the graft is thus placed in clean fascial tissue below the cutis, avoiding the extensive adipose tissue which is present in the axillary and groin region in the mouse. As a precaution against infection, the site of the inoculation was shaved and cleaned with alcohol and iodine. The trocar was inserted into the groin region and pushed upwards under the skin. The tumor graft was deposited

[1] From the Division of Cancer, Department of Hospitals, New York City, and the Department of Experimental Surgery, New York University Medical College. Read by title at the Twenty-ninth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-2, 1943.

midway between the groin and axilla by means of a plunger.

Thirty male mice about six weeks of age were divided among three separate cages, ten to a cage. Those of one group were implanted with tumor fragments irradiated with 5,000 r, those of another with tumor fragments irradiated with 60,000 r, and those of the third with non-irradiated tumor fragments. All of the mice were kept under the same conditions and received Purina dog chow and water *ad libitum*. Every twenty-four hours during ten successive days following implantation, tumor fragments were removed from three mice, one from each cage. This was done because of the previous observation that fragments of sarcoma 180 usually produced tumors about 1 cm. in diameter in ten days, while tumor fragments previously irradiated with 5,000 r produced no tumor but induced immunity which could be detected from ten days to six months after implantation, and tumor fragments irradiated with 60,000 r produced neither tumor nor resistance to subsequent implants. To avoid injury to the tumor grafts, special precautions were taken on their removal The skin was cut through the length of the mid-abdomen and lifted up carefully, being separated from the abdominal wall and thorax with the aid of a chromium spatula. The tumor graft was then seen lying attached to the skin. Measurements of the grafts were taken by means of a caliper before their removal from the animal. The tumor graft, including the surrounding tissue of the host, was dissected with sharp scissors, lifted up with fine forceps, and immersed in Zenker's fixative. This experiment was repeated, using the same number of animals and the same technic, with similar results. The sizes of the grafts as well as their macroscopic and microscopic characteristics are recorded in the appended Protocols.

OBSERVATIONS

Macroscopically, implants irradiated with 60,000 r (in air) did not appear appreciably different from those irradiated with 5,000 r (in air). They were pale—some yellowish—and attached to the skin of the host. No vascularity could be noted within the fragments, although capillaries and blood vessels could be seen in the periphery of the inoculation site. The tumors were between 2 mm. and 3 mm. in diameter, which approximated the initial size on implantation.[2] In contrast, the control implants appeared translucent and vascularized about the fourth day, while those examined on subsequent days had increased in size.

Microscopically it was observed that after irradiation with either 5,000 r or 60,000 r the implanted cells had undergone extensive degenerative changes. Some of the cells became pyknotic, with acidophilic cytoplasm. Others, especially in the later periods, showed irregularities of nuclear form with fragmentation or the occurrence of giant nuclei. Cytoplasmic vacuolization was often conspicuous. In the last few days of observation, implants irradiated with the larger dose contained less tumor tissue than those irradiated with the smaller dose, but cell counts were not made.

Necrosis was present in the central portion of the control implants during the first three days, decreased in amount during the resumption of active growth, and increased slightly during the last three days. Some of the peripheral cells did not undergo necrosis, and mitoses were noted among them on the third and subsequent days, during which increase in size of the implant occurred.

In the implants irradiated with 5,000 r, occasional mitoses were observed during the first two days. Whether this indicates that division started after implantation, or whether divisions present during irradiation were completed after implantation, is not determined. This question is of interest in view of the discussion in the literature concerning the dependence of

[2] A more precise procedure would have been to determine the weights of the implants. This, however, could not be done, because in dissecting the implants some of the surrounding normal tissue was included in order to avoid injury to the tumor graft.

induced resistance on the active growth of the implant.

It has been generally believed that the induction of resistance to transplanted tumors may be attributed either (*a*) to the growth or growth substances of the implanted tissue or (*b*) to its degenerative products. According to the observations made from this study, neither growth of the implant nor necrosis of its cells can alone account for the induction of resistance. The latter is clear from the failure of implants irradiated with 60,000 r to induce resistance, although necrosis is extensive. The former is suggested by the experiments of Sugiura (10) and others, who excised growing implants of sarcoma 180 and Flexner-Jobling rat carcinoma and found that resistance to subsequent implants had not been induced. Whatever induces resistance is operative after a dose of 5,000 r (in air) but not after 60,000 r (in air).

SUMMARY

After irradiation with 5,000 or 60,000 r (in air), implants of mouse sarcoma 180 showed no increase in size during ten successive days. Extensive degenerative changes were observed in the tumor cells, including nuclear pyknosis and fragmentation and cytoplasmic vacuolization. Tumor giant cells with pronounced cytoplasmic changes were often conspicuous.

Cytologic differences between the cells of implants irradiated with 5,000 r and with 60,000 r were not detected. During the last few days of observation the implants previously irradiated with 60,000 r contained a smaller amount of tumor tissue than those irradiated with 5,000 r.

Evidence that active growth occurred in the tumor implants irradiated with 5,000 r, which had previously been shown to induce resistance, was not observed.

PROTOCOLS

Macroscopic and Microscopic Characteristics of Implants During Ten Successive Days, Following Irradiation with 5,000 r (in air)

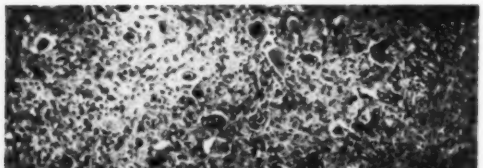
First Day: The tumor implant, measuring about 2 × 2 mm., slightly attached to the skin and imbedded in a gelatinous mass, was excised. Microscopic sections consisted of tumor, muscle, and fat. Tumor cells were seen in two sites: in the center of a pad of fat and at its periphery. (1) In the center of the pad of fat, they appeared as individual cells accompanied by a few leukocytes. These tumor cells showed no pyknosis. The nuclei had a distinct membrane and discrete chromatin particles; a few had prominent nucleoli. An occasional cell was binucleated, and an occasional one was in mitosis. In some, minute vacuoles appeared in the cytoplasm, sometimes limited to one part of the cell. These vacuoles were seen, also, in dividing cells. (2) At the periphery of the fat pad a few tumor cells were seen, surrounded by leukocytes. The tumor cells here showed pyknosis and nuclear details were not distinct. The chromatin particles were similar and more diffuse. Nucleoli were present, but indistinctly stained.

Second Day: The tumor implant, about 2 × 2 mm., appeared opaque, imbedded in a gelatinous mass attached to the skin. The microscopic picture showed a large necrotic mass with tumor cells at the periphery. The nuclei were often of irregular form. The cytoplasm was fairly abundant, sometimes vacuolated. An occasional mitotic figure was observed. In the tumor cells, nuclei tended to stain diffusely, with fewer discrete chromatin particles than in those of the first day. This was particularly noticeable near the central part of the necrotic area, where the cells became smaller and more pyknotic, and many underwent disintegration. There was an inflammatory reaction in the surrounding tissue, but this was not very intense.

Third Day: A 3 × 3-mm. tumor implant, pale, imbedded in a gelatinous mass, was dissected. The microscopic picture showed tumor, muscle, and adjacent fat tissue. The tumor cells were few and accompanied by edema and inflammatory reaction. They showed degenerative changes in the form of irregular nuclei, with diffuse nuclear staining and indistinct discrete chromatin particles. Vacuolization of the cytoplasm was prominent. Mitosis was not observed.

Fourth Day: The implant, approximately 2 × 2 mm., appeared opaque, imbedded in a gelatinous, non-vascular mass. Microscopic sections showed a fragment of tissue containing tumor giant cells, inflammatory corpuscles, and necrosis. The tumor cells all showed degenerative changes. Most had irregular nuclei or several nuclear lobes. The chromatin was finely divided, the nuclei often deeply stained. In some cells several small nuclear particles were seen. There was also vacuolization of the cytoplasm.

Fifth Day: The tumor implant, about 3 × 2 mm., appeared pale, but the gelatinous mass in which it was imbedded was vascular. Microscopic sections showed necrosis, with a chronic granulomatous inflammation in the surrounding tissue, containing large numbers of tumor giant cells. These



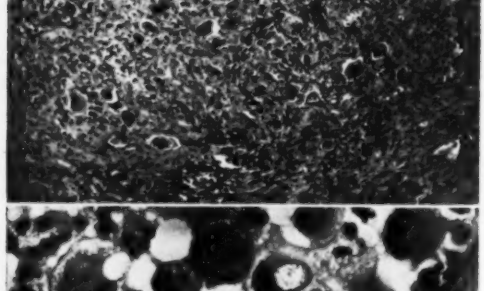


Fig. 1 (above). Tumor implant of sarcoma 180 six days after irradiation with 5,000 r (in air). Note the irregular shape of the nuclei of the sarcoma cells, the fragmentation of the chromatin substance, and the cell with the three-lobed nucleus. Hematoxylin and eosin. ×90.

Fig. 2 (below). Tumor implant eight days after irradiation with 5,000 r (in air). Note the swelling of the sarcoma cells, vacuolization of the cytoplasm, and nuclear irregularities. Hematoxylin and eosin. ×185.

tumor cells had sometimes a single nucleus and sometimes many nuclei. The nuclei were deeply stained. Only an occasional cell had a vesicular nucleus. Nucleoli were relatively prominent. Cytoplasm was abundant and often vacuolated. Mitotic figures were not observed in the tumor cells, but were present in the cells of the surrounding granulation tissue. In the cells with several nuclei, the appearance was often one of bleb formation, some of the blebs having been separated by constriction. Bleb formation of the cytoplasm was also occasionally seen.

Sixth Day: The implant, about 2 × 2 mm., was pale and attached to the skin. No blood vessels could be discovered in the immediate area. Microscopically there was seen a small mass of tissue, mainly granulation tissue, containing a large number of tumor cells. In many tumor cells the nucleus was vesicular, often irregular in shape; many showed chromatin fragmentation, while others had several small nuclear lobes. Cytoplasmic vacuolization was pronounced.

Seventh Day: The implant, about 2 × 2 mm., was firmly attached to the skin, opaque and pale. Microscopically, the mass of tissue was seen to contain numerous tumor cells, surrounded by mononuclear cells, some of which appeared to be phagocytes. Around this was an area of mild granulomatous inflammatory reaction, containing a few fragments of hair and foreign-body giant cells. All the cells showed degenerative changes of some type. Nuclear irregularities, with the formation of lobules or separate small nuclear fragments, were common. Pyknosis was present in some cells; others had vesicular nuclei, but with chromatin fragmentation. Nucleoli were only occasionally distinct. Cytoplasmic vacuolization was a prominent feature, and in many cells resulted in "foamy" cytoplasm. No mitoses were seen.

Eighth Day: The tumor implant, 3 × 2 mm., appeared opaque and pale, though it was surrounded by some blood capillaries. Microscopically a large mass of granulomatous tissue was seen, with a small amount of necrosis in the center. There were numerous tumor cells throughout the mass, showing various degenerative changes, including vacuolization of the cells and an occasional structure resembling an intranuclear inclusion. There were marked degenerative changes, as on the seventh day. The enlargement and vacuolization of the cytoplasm often produced large "foam" cells. Mitotic figures were not observed.

Ninth Day: The implant was pale and opaque, about 3 × 2 mm. The microscopic picture showed a mass of granulation tissue, in the center of which necrotic tissue appeared infiltrated with leukocytes. In the periphery, the cells were mainly of mononuclear type, although leukocytes were still present. In this mass, particularly in the mid-zone, were a number of very large tumor cells, some multinuclear, which apparently showed degenerative changes in the form of vacuolated cytoplasm, shreddy cytoplasm, and changes in nuclear shape. Some of the nuclei contained a single distinct rod-like nucleolus. Others were vesicular. Mitotic figures were not observed. An occasional foreign-body giant cell was also noted. An inflammatory reaction extended for a short distance into the neighboring muscle.

Tenth Day: The tumor implant, about 2 × 2 mm., was pale and opaque. The microscopic sections showed chiefly fibroblasts, mononuclear cells of various types, and occasional lymphocytes. Among these were a number of isolated large tumor cells, sometimes mononuclear, sometimes polymorphonuclear. The nuclei were occasionally hyperchromatic; some were greatly elongated. The cells themselves were often elongated, with cytoplasmic processes. Marked acidophilia of the cytoplasm was observed in a few of them. There was a distinct tendency for the large tumor cells to become elongated and to show pyknosis. Pyknosis was also ob-

served in several large polygonal tumor cells. There were no mitotic figures among the tumor cells.

Macroscopic and Microscopic Characteristics of Implants During Ten Successive Days Following Irradiation with 60,000 r (in air)

First Day: The implant, about 2 × 2 mm., was imbedded in a gelatinous mass. Microscopic sections showed necrotic tissue, with fragmentation of nuclei and leukocytic infiltration. There were isolated large tumor cells showing degenerative changes.

Second Day: The tumor implant, about 3 × 2 mm., was opaque, pale, and attached to the skin in a gelatinous mass. Microscopic sections showed necrotic tumor tissue, with dense leukocytic infiltration and nuclear fragmentation. At the periphery were a few tumor cells with slight pyknosis of the nuclei, distinct nucleoli, and moderate cytoplasmic vacuolization.

Third Day: The tumor fragment, measuring about 3 × 2 mm., was pale and attached to the skin. The microscopic picture showed a small piece of fat tissue with foci of tumor cells surrounded by inflammatory reaction. The tumor cells varied considerably in size and shape; some of the smaller ones were distinguished from fibroblasts with difficulty. The larger ones showed nuclear fragmentation or had very granular chromatin and loss of nucleoli. The cytoplasm of many tumor cells was vacuolated. Most of them were mononuclear, but a few were polymorphonuclear.

Fourth Day: The implant, about 3 × 2 mm., was pale and attached to the skin. Some of the microscopic sections showed only inflammatory reaction, consisting mainly of leukocytes and mononuclear cells. One of the slides showed, in addition, areas of necrosis; near these, and in them, were isolated cells which suggested tumor cells. They were large, irregular in shape, and some of them were hyperchromatic. Mitoses were not present.

Fifth Day: The implant, about 3 × 2 mm., appeared yellowish and opaque and was attached to the skin. Blood capillaries were not observed in the immediate area. The microscopic sections consisted of chronic inflammatory tissue, in which were several isolated, large, bizarre mononuclear and polymorphonuclear tumor cells. In some of the tumor cells the nuclear network was distinct, often granular. Some nuclei showed diffuse staining, and some had nuclear blebs or separate nuclear fragments. The cytoplasm was markedly vacuolated. An occasional giant tumor cell, with several nuclei, was seen. No mitotic figures were observed.

Sixth Day: The tumor implant, 2 × 2 mm., appeared pale and was attached to the skin. No blood vessels could be seen in the surrounding area. The microscopic sections consisted of granulation tissue in which degenerating tumor cells were seen. The large tumor cells were of irregular shapes, with polymorphous nuclei, occasionally with distinct nucleoli. In a few, the nucleus was hyperchromatic.

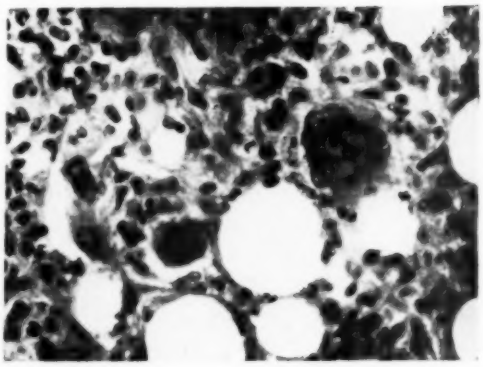


Fig. 3. Tumor implant six days after irradiation with 60,000 r (in air). Note the large irregular sarcoma cells, the polymorphous nuclei, and the vacuolated cytoplasm. Hematoxylin and eosin stain. ×185.

The cytoplasm showed small and large vacuoles. The surrounding inflammatory reaction consisted of a few leukocytes, but mostly small mononuclear cells and fibroblasts. This involved some of the surrounding striated muscle.

Seventh Day: A pale implant, about 2 × 1.5 mm. in size, attached to the skin, was dissected. Microscopically it consisted of a few very large cells, of bizarre form, surrounded by a chronic inflammatory reaction. The nuclei of these cells were larger, and the chromatin particles coarser, than in the normal tumor cells; some of the nuclei were polymorphic. Nucleoli were present, but only occasionally prominent. Other changes included pyknotic or granular nuclei, loss of nucleoli, and vacuolated cytoplasm.

Eighth Day: In size and macroscopic appearance the implant was similar to those previously described. Microscopic sections showed a minute nodule in which a few very large, bizarre tumor cells were seen. With these cells was a fibroblastic reaction forming a small granuloma, in the center of which a few foreign bodies were seen. The tumor cells showed nuclear granularity, with loss of nucleoli in some, and enlargement with irregular shape in others. In a few there was complete nuclear disintegration. Cytoplasmic vacuolization was pronounced.

Ninth and Tenth Days: The macroscopic and microscopic appearances of the implants on the ninth and tenth day following implantation were similar to those previously described. All tumor cells showed pyknosis or poorly stained nuclei, vacuolated and distintegrated cytoplasm. No mitotic figures were noted.

Macroscopic and Microscopic Characteristics of Unirradiated Control Implants During Ten Successive Days

First Day: The implant, about 2 × 2 mm., was imbedded in an opaque, gelatinous mass. In the

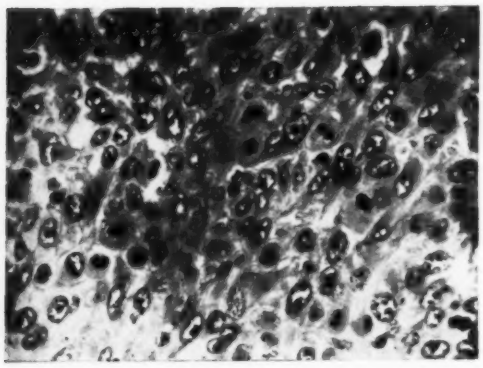


Fig. 4. Section of a tumor produced by a control non-irradiated implant. Note the numerous mitotic figures and the abunpance of actively growing cells, in contrast to the previous figures. Hematoxylin and eosin stain. ×185.

serial sections, the tumor cells showed varying degrees of nuclear hyperchromatism, the most marked changes resulting in small, densely stained nuclei. There was a progressive loss of the nucleoli as these changes became more marked. The cytoplasm was often vacuolated, and in some instances contained fragments of eosinophilic material. In cells with the greatest nuclear changes, the cytoplasm had become homogeneous and deeply eosinophilic. In addition, some cells showed karyolytic changes resulting in faintly stained "ghost-like" remnants. No mitoses were observed.

Second Day: The implant was attached to the skin, surrounded by an opaque, gelatinous mass, in which a few blood capillaries could be seen. Microscopically, there could be noted a necrotic portion of the tumor implant, inflammatory corpuscles, granulation tissue, and a few tumor cells at the periphery. The morphologic appearance of the tumor cells was similar to that on the first day.

Third Day: The implant, about 3 × 3 mm., was attached to the skin and surrounded by a gelatinous, vascular mass. In the central area the cells were completely necrotic. The outer zone of tumor tissue contained well preserved cells; many were elongated, with long cytoplasmic processes. Except for this difference in shape, there was considerable uniformity in their appearance. The nuclei were vesicular, with distinct nuclear membranes. Chromatin particles were, in general, small and were often more prominent in the peripheral areas than in the center of the nucleus. There was usually one prominent nucleolus, which was round or elongated. There were approximately two mitoses per high-power field in the center zone of the implant. Giant cells were present, but not conspicuous.

Fourth Day: The implant, about 3 × 3 mm., appeared transparent, surrounded and penetrated by blood capillaries. Microscopically there could be seen a mass of tumor tissue with a large central necrotic area. The tumor cells showed a number of mitotic figures, as well as multinucleated giant cells. The tumor cells infiltrated the surrounding fat in a rather diffuse manner. There was a moderate amount of edema.

Fifth Day: The implant, about 4 × 3 mm., was transparent and vascular. Serial sections showed tumor tissue with a necrotic area in the center. A number of fibroblasts were seen around the tumor.

Sixth Day: The implant, about 4 × 4 mm., appeared transparent and vascular. The microscopic sections showed chiefly well preserved tumor cells. Mitotic figures were present. There was a moderate infiltration of leukocytes and lymphocytes within the tumor. In the center was a small area of necrosis.

Seventh Day: The tumor, about 8 × 6 mm., appeared vascular. It was attached to the skin but was easy to remove. Microscopically there could be seen a mass of tumor tissue with a necrotic center. At the edge of the necrosis there were numerous fibroblasts. The tumor cells occasionally had giant forms. Mitotic figures were present.

Eighth Day: The size of the tumor was 9 × 6 × 5 mm.; it was vascular, encapsulated, and easy to remove from the skin. The microscopic picture showed a compact mass of tumor cells, varying slightly in size and appearance. Most of the cells were somewhat irregular in shape and were slightly separated, with cytoplasmic processes. The nuclei were moderately clear, with distinct nuclear membranes and a number of small chromatin particles. The nucleoli were sometimes, but not always, fairly distinct. Mitotic figures were numerous. The cytoplasm was slightly stained with eosin; staining was in some instances more distinct near the nucleus than at the periphery. In a few areas there was focal necrosis, in which the tissue had undergone degeneration, and numerous small irregular nuclear fragments were seen. The cells at the periphery of the necrotic area showed degenerative changes in the form of pyknosis of the nucleus and increased acidophilia of the cytoplasm. Occasional vacuoles in the cytoplasm were seen in these areas, and small round acidophilic globules were present in some of the vacuoles. The tumor infiltrated the surrounding fat tissue.

Ninth and Tenth Days: The tumors at the ninth and tenth days after implantation into the animals varied between 0.9 and 1.0 cm. in diameter. The microscopic pictures were similar to that on the eighth day.

The four photomicrographs which are included in this paper serve as typical examples to illustrate the cellular appearance of the implants irradiated with 5,000 r (in air), 60,000 r (in air), and the unirradiated controls.

My grateful appreciation is herewith expressed to Dr. G. L. Rohdenburg, Director of Laboratories, Lenox Hill Hospital, New York, formerly associated

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X-Ray Growth Zone Studies in the Rat Tail for the Appraisal of Chondrotropic Effects[1]

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INDICES OF growth commonly are determined by the size and weight of the experimental animal without reference to the specific components contributed by the separate organs or tissues of the body. Growth hormones in the past have been appraised by their effect on body weight, whereas better standardization might have been obtained by the use of tables based on observations of the "growth mechanism" of bones. The effect of hypophysectomy, causing cessation of cartilage plate proliferation, had been recognized, but not until it was re-emphasized by such observers as Freud, Levie, and Kroon (9), was it made clear that the terms "growth hormone" and "chondrotropic hormone" should be used synonymously.

The histologic study of chondrotropic effects in bone growth zones can be a long or a tedious procedure, while the x-ray examination of growth acceleration or arrest, without sacrifice of the growing parts to histologic study, can be accomplished rapidly. If both methods were to be combined, as Guerrant and Dutcher (10) actually have done in their "line test" examinations of rat tails, perhaps the optimum amount of information could be obtained. Levie (12) used the roentgen examination of the rat's tail for studying bone growth, but his standards and growth tables leave much to be desired. By a thorough reinvestigation of this method, it was our hope that a more reliable x-ray index of normal bone growth could be established as a reference for the assay of growth hormones or for the appraisal of abnormal bone growth due to any cause.

METHOD

Accurate measurements of tail length were made directly from the x-ray film; this was possible because the rats were placed in the supine position with the tail next to the film to prevent distortion. To get the best detail, the exposure time was reduced to 1/20 of a second, and fine-grain screens, a small cone, and a film-target distance of 48 inches were used. Some exposures were made without screens, but these films were not found superior enough in detail to make up for the advantage of better contrast offered by the use of screens. Of prime importance in the demonstration of all the growth zone details are films which have the proper density of exposure.

The reproductions in this paper, particularly Figure 3 show the characteristics of both properly and improperly exposed films. Errors of overexposure, if not too great, can be compensated by variations in the intensity of light in the viewing apparatus, whereas even slight degrees of underexposure result in films which fail to reveal the finer details in structure and outline of both bone and cartilage plates.

In counting the number of tail segments, the first proximal segment was designated as that one just distal to a line drawn through the lowermost margins of the ischii. The sacro-caudal segments in this area often appear slightly distorted because of the hyperextension which occurs at this level of the spine when the rat is held supine against the film. This sometimes not only makes selection of the first tail segment difficult, but also interferes with good visualization of the structural details. Some distortion of this area in the lateral view also is unavoidable, because the spine in the tail is not in the same plane with the dorso-lumbar spine when the animal is placed in this position. The use of light ether anesthesia, as practised

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by Levie (12), was not found necessary, because of our use of a short exposure time.

More than 1,200 rats were examined for this investigation. By the kind permission of the Wistar Institute, their entire colony

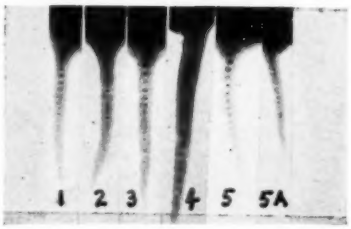

Fig. 1. Rat tail growth during first 5 days after birth. Daily length increments average 3.0 mm., but vary from 1.5 to 4.5 mm., depending on the size of the animal at birth and on the modifications in growth rate due to hereditary, dietary, and seasonal factors.

was studied. This afforded us data on different litters of various ages. Similar Wistar stock rats in our own laboratory were studied daily from birth until two years of age, in order to round out the sources of our data.

RESULTS

Day of Birth: The tails average 1.5 to 2.0 cm. in length, and the number of calcified tail segments varies from 7 to 9. The 2 proximal segments each have two unfused primary centers of ossification. The cephalic bodies are quadrilateral and become progressively flatter distally until the terminal 2 or 3 resemble thin transverse lines.

Second Day: There are 10 or 12 calcified segments, and the length of the tail varies from 1.8 to 2.3 cm.

Third Day: The number of calcified segments varies from 14 to 16, and the tail length from 2.0 to 2.7 cm. Thin transverse lines often are seen through the middle of the proximal 3 bodies, which also have transverse processes.

Fourth Day: The number of calcified segments totals 15 to 17, and the tail length varies from 2.5 to 3.1 cm. A thin transverse line may be seen in the proximal 4 or 5 bodies. The primary centers of ossification of the proximal 2 segments are fused.

Fifth Day: There are 17 to 19 calcified segments in the tail, which varies from 2.7 to 3.3 cm. in length. Mid-transverse body

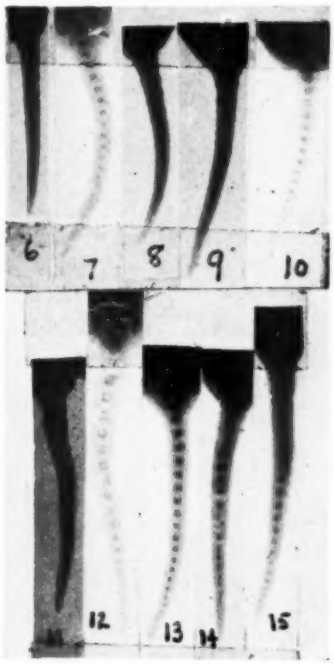

Fig. 2. Rat tail growth between the 6th and 15th day.

lines may be seen in the proximal 5 or 6 segments.

Sixth Day: The tail ranges from 2.9 to 3.6 cm. in length and contains 18 to 20 calcified segments. A mid-transverse line or a central minute calcified nucleus appears in each of the proximal 6 to 10 bodies.

Seventh Day: The tail is comprised of 20 to 22 calcified segments and varies from 3.3 to 4.0 cm. in length. Mid-transverse lines or central nuclei are visible in the cephalic 8 bodies.

Eighth Day: Twenty-one to 23 calcified segments are visible, and the length of the tail ranges from 3.7 to 4.2 cm. A calcified central nucleus or a mid-transverse line is discernible in the proximal 8 or 9 bodies.

Ninth Day: The length of the tail varies

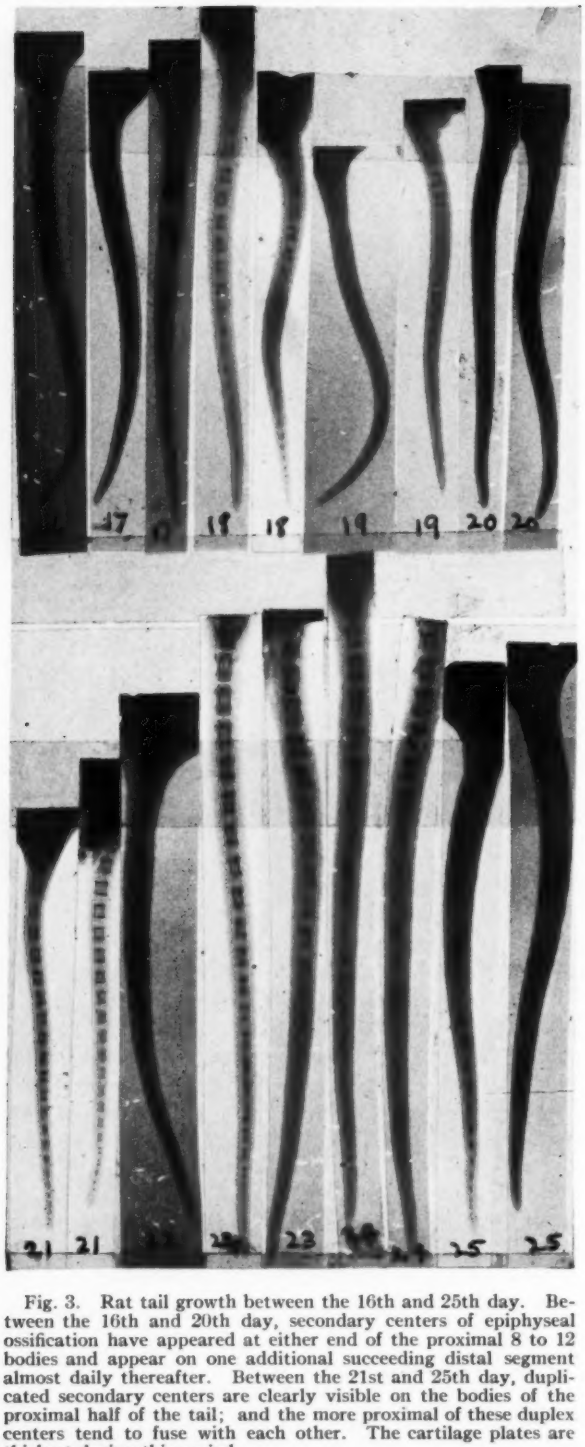

Fig. 3. Rat tail growth between the 16th and 25th day. Between the 16th and 20th day, secondary centers of epiphyseal ossification have appeared at either end of the proximal 8 to 12 bodies and appear on one additional succeeding distal segment almost daily thereafter. Between the 21st and 25th day, duplicated secondary centers are clearly visible on the bodies of the proximal half of the tail; and the more proximal of these duplex centers tend to fuse with each other. The cartilage plates are thickest during this period.

from 4.2 to 4.6 cm. and 22 calcified segments may be visible.

Tenth Day: Twenty-three calcified bodies may be seen, and the tail is 4.4 to 4.9 cm. in length. A mid-vertical instead of a mid-transverse line or a central nucleus may be seen in the proximal 8 bodies.

Eleventh Day: The tail length varies from 4.6 to 5.0 cm., but it is comprised of not more than 23 calcified segments.

Twelfth Day: Twenty-four calcified segments are present, and some semblance of a cancellous structure is visible in the proximal 8 to 10 bodies. The tail length varies from 4.9 to 5.3 cm.

Thirteenth Day: The tail length ranges from 5.1 to 5.7 cm., and the number of calcified segments varies from 23 to 25.

Fourteenth Day: Calcified segments number 25, and a central nucleus or cancellous lines can be visualized in the proximal 18 segments. The tail varies from 5.3 to 6.1 cm. in length.

Fifteenth Day: The tail ranges from 5.4 to 6.5 cm. in length and is comprised of 24 to 26 segments. In about 10 per cent, faint calcification of secondary centers of epiphyseal ossification appear at either end of the proximal 2 or 3 bodies. Each of these centers is comprised of two separate nuclei as seen in the anteroposterior view. Longitudinal cancellous lines are visible in the bodies of the proximal 12 to 14 segments, and central nuclei in the succeeding 4 to 6 bodies.

Sixteenth Day: The tail length varies from 5.5 to 6.7 cm., and the number of calcified bodies from 25 to 27. In about 15 per cent of rats, secondary centers of epiphyseal ossification are visible at either end of the proximal 3 or 4 bodies, each comprised of two separate nuclei.

Seventeenth Day: The tail measures 5.6 to 7.2 cm. in length, the number of calcified segments totals 25 to 27, and duplicated secondary centers of epiphyseal ossification are present in the proximal 5 segments in about 50 per cent of the rats. Two apophyseal centers are visible near the distal ventral corners of each of the proximal 3 bodies, best seen in oblique or lateral views. Cancellous architecture may be seen in the proximal 12 to 20 bodies.

Eighteenth Day: The number of calcified bodies in the tail is 25 to 27, and secondary centers of epiphyseal ossification are seen in the proximal 5 to 7 segments. These centers are usually duplicated, although those of the proximal 2 bodies may be fused with each other to form a single thin plate. Distal ventral apophyses are present in the cephalic 3 segments, and the tail length ranges from 5.7 to 7.5 cm.

Nineteenth Day: The tail measures 5.9 to 7.8 cm. in length and there are 25 to 27 calcified segments. Duplex centers of epiphyseal ossification are present at either end of the proximal 8 to 12 bodies. The more proximal of these tend to form a single plate by fusion with each other. Cancellous structure is more definite in the proximal bodies, and this is better seen usually in the lateral view.

Twentieth Day: The length of the tail averages 6.0 to 8.3 cm., and the number of bodies with secondary centers of epiphyseal ossification is from 10 to 12. The proximal bodies are taking on a more adult form and the vertical and transverse body lines are often duplicated, indicating the beginning of adult cancellous architecture.

Twenty-first Day: The tail is comprised of its maximum number of calcified segments, 26 to 28. Secondary centers of epiphyseal ossification are visible in the proximal 10 to 14 bodies and the distal 5 to 7 are duplicated. The bodies now tend to lose their straight contours and to become slightly biconcave along their longitudinal margins. The tail length ranges from 6.1 to 8.5 cm.

Twenty-second Day: The length of the tail varies from 6.3 to 8.9 cm. and the number of bodies with secondary centers of epiphyseal ossification from 12 to 16. The tail otherwise has the same characteristics as on the 21st day.

Twenty-third Day: The tail has now lengthened to 6.6 to 9.3 cm., and 13 to 17 proximal bodies bear secondary centers of epiphyseal ossification.

Twenty-fourth Day: The tail measures

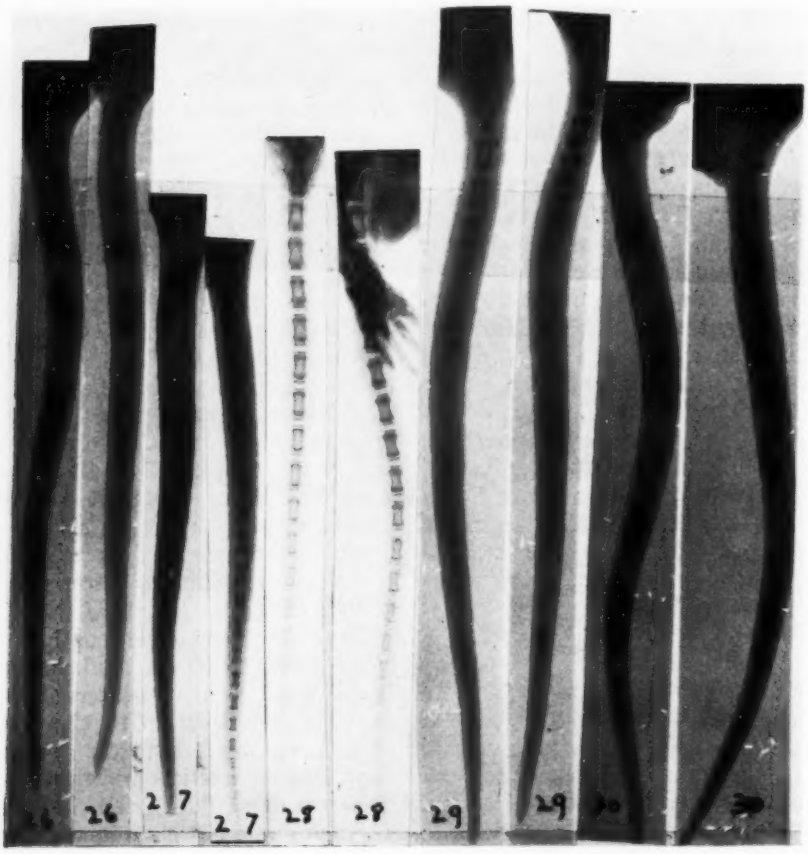

Fig. 4. Rat tail growth between the 26th and 30th day. Fusion has occurred in all the duplex centers of epiphyseal ossification except those on the distal 2 or 3 bodies, where they have but recently appeared.

7.1 to 9.7 cm. in length, and 14 to 18 proximal bodies bear secondary centers of epiphyseal ossification.

Twenty-fifth Day: The appearance of the tail is similar to that of the 24th day, but its length has increased to 7.3 to 9.8 cm. The cortex of the proximal bodies begins to get thicker.

Twenty-sixth Day: The number of bodies with secondary centers of epiphyseal ossification has increased to 16 to 20, and the centers in more than half of the proximal segments have fused with each other to form single thin plates.

Twenty-seventh Day: The tail is 7.9 to 10.5 cm. in length; otherwise it resembles the tail of the 26th day.

Twenty-eighth Day: The number of bodies with secondary centers of epiphyseal ossification is 17 to 21, and the tail length is 8.2 to 11.0 cm.

Twenty-ninth Day: There are 19 to 23 bodies with secondary centers of epiphyseal ossification, and the tail ranges from 8.5 to 11.5 cm. in length. The bodies have an adult configuration, and in those of the proximal half of the tail distinct cancellous structure may be seen.

Thirtieth Day: The tail measures 9.0 to 12.0 cm. in length; otherwise, it has a similar appearance to the tail of the 29th day.

Thirty-second Day: The tail measures 9.5 to 12.4 cm. in length, and there is dis-

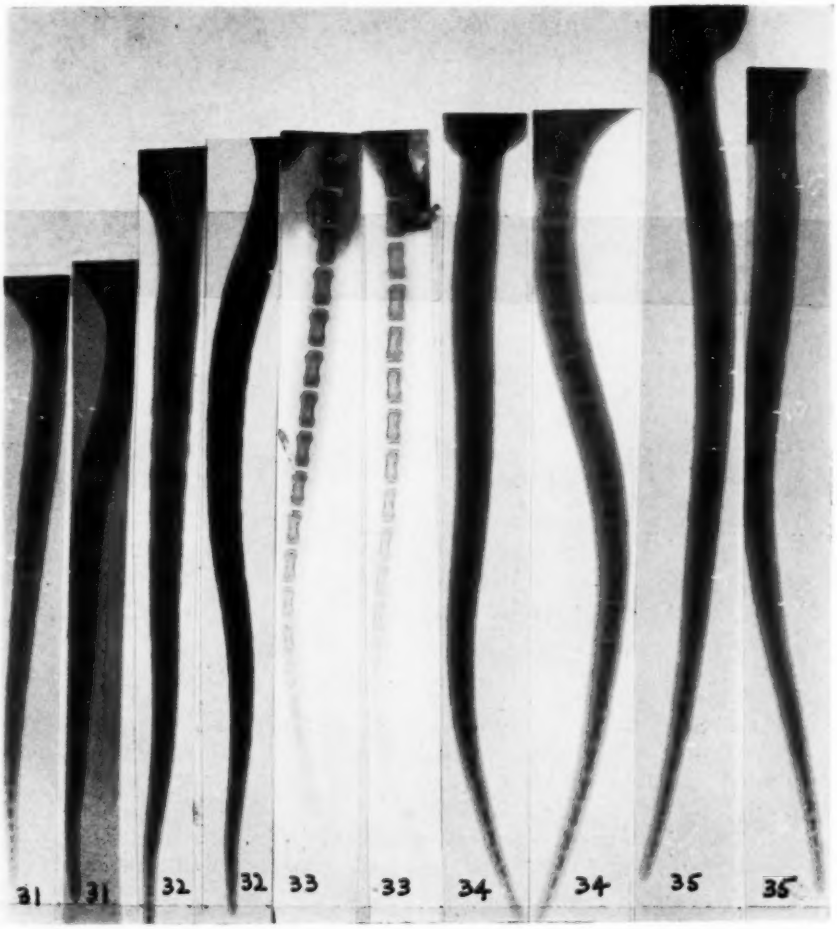

Fig. 5. Rat tail growth between the 31st and 35th day.

tinct cancellous structure in the more proximal bodies.

Thirty-fifth Day: The tail length varies from 9.7 to 13.5 cm., and the number of bodies with secondary centers of epiphyseal ossification ranges from 21 to 23. Only the secondary centers of the distal 3 or 4 bodies remain duplicated. The margins of the bodies appear more concave in the lateral view than in the anteroposterior view; and in the lateral view, the ventral margin of each body is more concave than the dorsal margin.

Fortieth Day: The tail is 10.7 to 14.7 cm. in length, and the number of bodies with secondary centers of epiphyseal ossification varies from 22 to 24. The epiphyseal cartilage plates of the proximal 5 to 10 bodies now have reached almost their ultimate degree of thinness, suggesting that the initial stage of retarded growth and lapsing has begun.

Forty-fifth Day: The length of the tail is 13.4 to 15.9 cm., and all bodies but the last 2 have secondary centers of epiphyseal ossification. On the tips of the transverse processes of the proximal 2 or 3 bodies are visible new secondary centers of epiphyseal ossification. Distal ventral apophyses are visible in the proximal 8 to 14 segments.

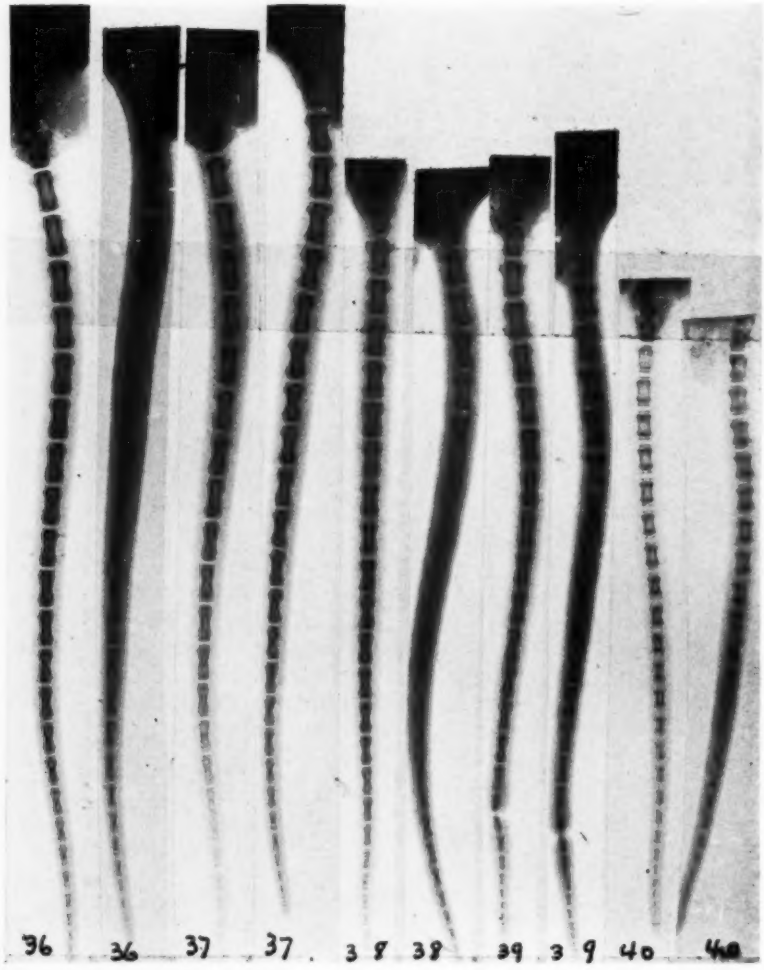

Fig. 6. Rat tail growth between the 36th and 40th day.

having made their first appearance during the preceding one to three days. New centers are also visible at the tips of the spinous processes of the proximal 4 to 10 bodies.

Fiftieth Day: All but the distal 1 or 2 bodies reveal secondary centers of epiphyseal ossification; distal ventral apophyses are present in the proximal 10 to 16 interspaces; and on the proximal 10 to 14 spinous processes and on the transverse processes of 8 proximal bodies, secondary centers of epiphyseal ossification are to be seen.

Sixtieth Day: There are secondary centers of epiphyseal ossification on all bodies except the distal 1 or 2 segments, on the proximal 10 to 14 spinous processes, and on the proximal 6 to 11 transverse processes. The tail length ranges from 15.8 to 17.5 cm. Lapsing seems to have occurred in the epiphyses of the proximal 8 to 10 segments, in which the cartilage plates have reached a degree of thinness characteristic of final growth retardation.

Seventieth Day: There are secondary centers of epiphyseal ossification on the proximal 26 to 28 bodies. Pairs of distal

Fig. 7. Rat tail growth between the 45th and 100th day. During this period, lapsing of bone growth occurs progressively from the proximal to the distal segments.

ventral apophyses number 18 to 20; there are centers at the tips of the transverse processes on 18 to 20 segments and at the tips of the spinous processes of the proximal 16 to 17 segments. The length of the tail varies from 16.5 to 18.5 cm.

Eightieth Day: Secondary centers of epiphyseal ossification are visible at the ends of all the bodies except the last 1 or 2, at the tips of the transverse processes of the first 10 or 12, of the spinous processes of the first 16 or 17, and in the distal ventral apophyses of the proximal 19 or 20 segments. The tail measures 16.5 to 19.2 cm. Lapsing of the main secondary centers of epiphyseal ossification seems to have occurred in the proximal 10 to 16 segments.

Nintieth Day: The appearances are practically the same as on the 80th day.

One Hundredth Day: There are pairs of distal ventral apophyses of 22 to 24 proximal bodies. The tail length varies from 17.5 to 19.5 cm. Lapsing of the main secondary centers of epiphyseal ossification of all but the distal 5 to 8 segments seems to be present.

From the 100th day to the end of the second year, there are no changes in the number of secondary centers of epiphyseal ossification or in the length of the tail. No actual bony fusion of the epiphyses with the bodies is observed, but the centers seem to become more compact and organized. The cartilage plate between the epiphysis and diaphysis becomes only slightly if at all thinner, except in the terminal 2 to 6 segments, where the cartilage plates remain thicker than those of the more proximal segments, and final lapsing does not seem to occur in them until well along into the second year.

DISCUSSION

The tail measures 1.5 to 2.0 cm. at birth, and during the first three weeks the length increases approximately 2 to 4 mm. daily. In the following weeks, the daily increment in length tends to become less, averaging 1.5 to 3.0 mm. The full length of the tail is reached about the 100th day and varies from 17.5 to 19.5 cm.

The first secondary centers of epiphyseal ossification at either end of the bodies of the proximal 4 or 5 segments appear on or about the 15th day after birth. Each successive day is marked by the appearance of additional centers on one or two succeeding distal segments until, on the 45th day, they appear on all but the terminal one or two segments. The size and shape of these centers change with the growth of the animal. At their first appearance, each center is usually comprised of two isolated nuclei as seen in the anteroposterior view. In the lateral view, these duplicated nuclei are not visible because they are separated by a cleft in the sagittal plane. There may be some irregularity of the nuclear margins in the lateral view, but this is due to lack of uniform calcification. These isolated nuclei of the epiphysis are almost circular when first seen in the anteroposterior view, but with each successive day, they tend to flatten as they extend and approach each other toward the mid-line. On the 7th to the 10th day after their first appearance, they fuse with each other to form a thin disk, slightly convex on the articular side and more or less irregular along the margin bordering the epiphyseal cartilage. For a few days prior to complete fusion, when only a thin bridge of calcification unites the nuclei, these epiphyseal plates have a dumb-bell shape. During the following days, the mid-line defect fills in until the thickness of the epiphyseal disk is almost uniform. After the 25th day, in the anteroposterior view, there appear V-shaped epiphyseal tenons which fit into diaphyseal mortises near the edges of the epiphyseal plates. In the lateral view, a similar pair of tenon-mortise contours may be seen, but not so close to the edges as in the anteroposterior view. About the 80th day, the bony surfaces bounding the cartilage plates begin to get smoother, and on about the 100th day they are quite smooth.

During the succeeding days and weeks, there is no appreciable change in the thickness of the cartilage plates themselves except in the terminal 2 to 6 segments;

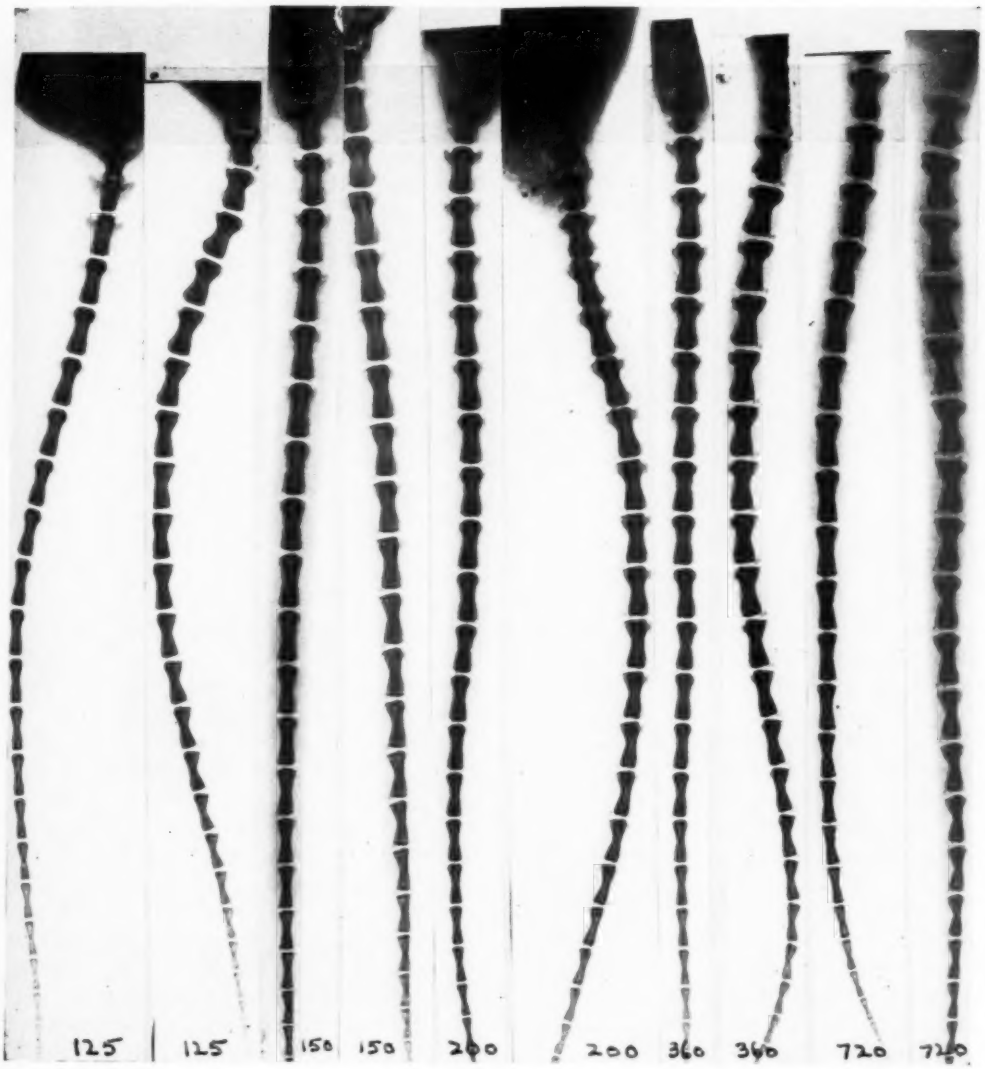

Fig. 8. Rat tail growth from the 125th to the 720th day. There has been lapsed retardation of bone growth during this period, the cartilage plates remaining visible, but thin and discontinuous.

under magnification with a reading hand lens,[3] one can make out thin, compact osteosclerotic bounding zones on either side of these plates. These parallel sclerotic zones bounding the cartilage plate can be seen only in those segments where the central ray of the roentgen beam traverses the zones tangentially. Since the central ray is aimed at the mid-tail, it is only in these segments that the bounding zones of osteosclerosis may be seen. In the adult rat tail, there is slight kyphotic inclination of the articular surfaces of each body, which accounts in part for failure to obtain tangential views of all zones in a single film.

At the tips of the spinous processes, secondary centers of epiphyseal ossification first appear in the proximal 10 to 12

[3] Between 10 and 100 diopters.

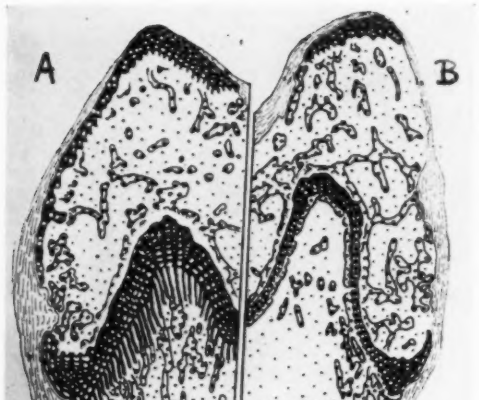

Fig. 9. A. Active bone growth. B. Lapsed bone growth. After Nunnemacher.

segments on or about the 45th day after birth. On the 50th day, they have increased in number to include the proximal 13 to 18 segments, where they remain visible during the remainder of the first two years of life.

Pairs of detached apophyses resembling sesamoids appear near the distal ventral articular margins of the first 12 to 15 bodies on or about the 45th day after birth and, gradually, on more distal bodies, so that by the 70th day they are apt to be seen on the proximal 18 to 22, where they remain visible permanently.

At the tips of the transverse processes, secondary nuclei first appear on 2 or 3 proximal divisions on the 46th day; they are visible on the proximal 10 to 12 segments on the 50th day. Around the 250th day, only 7 or 8 may be visible, but even at the end of the first year, 5 to 7 can usually be seen. These nuclei possibly are nothing more than extensions lateralward of the proximal epiphyseal plates, but the connecting bridges are not always visible, thus giving these centers their detached appearance.

Levie (12) found that the body weight, body length, and tail length did not run parallel as growth indices. No attempt was made in our studies to check these conclusions, but we did find that there is considerable normal variation in tail length, probably influenced by such factors as the number of rats in a litter and hereditary, dietary, and seasonal differences. For these reasons, it would seem highly desirable that these factors be reckoned with when undertaking studies of the chondrotropic effects of any test substance.

Strong (19) and Dawson (3) have shown that cartilage plates fall into two pronounced groups: (1) those which become inactive and disappear by the 150th to 180th day, allowing the epiphysis to unite with the shaft; (2) those which become inactive and remain in a lapsed condition until senility. A corresponding state of lapsed cartilage plate activity without actual bony fusion does not occur normally in man except in the lambdoidal and sagittal sutures of the skull (20).

Dodds (4) found that cartilage plates reveal no visible differentiation at birth but, by the 7th day, the cartilage cells become oriented into typical row formation between the diaphysis and epiphysis. By the 14th to the 18th day, the diaphyses and epiphyses are well formed. The cartilage plate then has five zones. Zone I is the layer in the epiphysis just distal to the cartilage plate, where, scattered in the matrix, are reserve cells which divide and give rise to the "mother row cells" in a comparatively thin zone. Zone II, next in line toward the diaphysis, reveals generally the thickest cell multiplication. Here the "mother row cells" undergo two divisions, with short rows of four cells each. These short rows lie end to end to form the long columns characteristic of the cartilage plate. The cells in this zone are normally flat, so that the plane of mitotic division is parallel with the rows. The lengthening of bone is caused by these divisions. Proceeding proximally, in Zone III the former flat cells become cuboidal. In Zone IV, the cartilage cells become fully developed and then are destroyed by the invading capillaries from the diaphyseal marrow. Calcification also occurs in the matrix between the cell rows. In Zone V, enchondral bone

is laid down as cartilage removal progresses, forming projecting trabeculae. These five zones can be delimited clearly (13).

In the stage of lapsed union, trabeculae on the diaphyseal side of the cartilage plate are absent and there are, instead, smooth layers of lamellate bone on both sides of the cartilage plate which are quite thin. In this same phase of lapsed activity, the cartilage rows become short and sparse, with large patches of dense fibrillar matrix between them. Silberberg and Silberberg (16) noted that the cartilage plate gets progressively narrower in the upper tibia from about the 55th day. They found that by the end of four or five months it was only half its original width, and that, by the eighth or ninth month, only a thin sclerotic line of euhyaline cartilage could be seen delimited toward both the epiphysis and diaphysis by a layer of bony tissue. Even in the third year of life, they found rudimentary cartilage and calcium deposits in the epiphyseal plate, which was by that time transformed into a thin, sometimes discontinuous, transverse plate containing scanty remnants of cartilage. Thus, no evidence of actual bony epiphysio-diaphyseal union was found to have occurred. It was also found in the mouse that active growth proceeded for about 120 days, when proliferative activity ceased and retrogressive processes set in, characterized by atrophy, degeneration, and calcification of the epiphyseal cartilage.

Silberberg and Silberberg quote similar observations by Dawson in the rat and they make the pertinent observation that at no time did they note vascular perforations of the epiphyseal cartilage, as in man or dog, where at the initiation of ossification in the epiphysis, osteogenic invasions from the diaphysis are readily observed. In old rats, Dawson (2) found that the final obliteration of the cartilage, when it does occur, appears to be the result of transformation of the residual cartilage by metaplasia rather than by destruction, succeeded by bony substitution. In man, Dawson further pointed out, growth in the length of a bone, due to the activity of the epiphyseal cartilage plate, may cease long before the cartilage plate itself is obliterated and, for some reason not clearly understood, the final differentiation of this zone is delayed. In the rat, in those areas, as the olecranon, femoral head, distal femur, proximal tibia, distal radius, humeral head, scapula, pelvic margins, and tail, where the cartilage of conjugation persists throughout life, Dawson found it impossible, due to the extreme variability of the histologic pattern, to determine any definite age at which it could be said with certainty that growth had ceased and union or differentiation had become retarded.

Levie (12), on the other hand, claimed that in the rat, the proximal 12 secondary centers of epiphyseal ossification in the tail fused on the 55th day and that from the 70th to the 119th day progressive fusion of the distal segments occurred. Our findings substantiate these observations. It was evident to us that lapsing of the tail epiphyses begins in the proximal segments about the 45th day and progressively involves more segments daily thereafter until the 100th day, when lapsing of all but the last 2 or 3 segments has occurred. Much of each cartilage plate between the diaphysis and epiphysis can be seen in the roentgenograms for the remainder of the rat's life, even though these plates may be thin, discontinuous, and of varying densities.

Faulty sectioning and staining may lead to unwarranted conclusions about the persistence and disappearance of the cartilage plate. Silberberg and Silberberg (16) pointed this out in the mouse, in which the first stage of epiphyseal proliferation is followed after 120 days by the second stage, characterized by atrophy, degeneration, and calcification of the epiphyseal cartilage; the localized degenerated areas in the epiphyseal zone, originating by coalescence of several degenerated cartilage cell rows, are then the areas which may lead to trouble in diagnosis. The Silberbergs pointed out that Schmorl (15) called these areas "Ossifikationslücken,"

assuming that no calcification could take place in them; that Erdheim (5) considered these areas foci of calcification to brace the excessive amount of soft cartilage formed in acromegaly, and that Böhmig (1) defined them as sites of degeneration which later underwent ossification as a result of a disturbance in growth. The Silberbergs considered all these changes normal, as part of the process of epiphyseal lapsing, so that it seems warranted to say that the *sine qua non* in the appraisal of chondrotropic effects is a thorough knowledge of these normal but variable microscopic appearances.

Other important observations made by the Silberbergs in the mouse which are applicable to the rat, as shown by Hammett (11), Spark and Dawson (17), are that the female reveals the epiphyseal proliferative process of the first stage of cartilage growth two or three weeks in advance of the male, and that the male is earlier than the female in revealing the characteristic changes of the third stage of lapsing. They also pointed out a strain difference in the time schedule of the stages of proliferation and lapsing of the growth centers, and they were inclined to attach significance to these findings in so far as signs of more rapid aging of the growth centers occurred in mice strains with a natural high incidence of mammary cancer, possibly due to excessive estrogens. These fine histologic variations probably cannot be demonstrated in roentgenograms and these important limitations of roentgenography must be considered in planning methods for studying chondrotropic effects. On the other hand, Dawson (2) found an inconstant variation of retardation of bony epiphyseal fusion in many individual rats, so that it is obvious, in studying chondrotropic effects, that large numbers of animals must be observed; this could be accomplished more readily by roentgen than by histologic methods.

For the bioassay of pituitary growth hormones, Evans, Simpson, Marx, and Kibrick (7) used 26-day-old female rats, which they injected with the hormone of unknown potency for four days beginning on the 12th day after hypophysectomy. By a rapid staining method, they could measure the thickness of the proliferating cartilage plate under a microscope with a calibrated micrometer eye-piece. By comparing with controls, they worked out criteria for bioassay of the pituitary hormones. It would be interesting to compare their method with roentgen procedures such as are suggested in this report, employing a fixed scale of magnification with a low diopter lens.

SUMMARY

1. X-ray growth zone studies were made of a large number of tails of Wistar rats from birth until two years of age.

2. A description is given of the daily variations of the bodies and secondary centers of epiphyseal ossification as seen in the roentgenograms.

3. The histologic pictures of the growth zones in normal rats and mice are reviewed and compared with the roentgen characteristics.

4. A growth calendar is suggested, which could be used to study chondrotropic effects.

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Depth and Exit Doses for Various Phantom Thicknesses[1]

M. C. REINHARD, M.A., and H. L. GOLTZ, B.S.
Buffalo, N. Y.

WHEN APPLYING depth dose values for treatment purposes, the thickness of the phantom used in determining the dose at depth is frequently ignored. That this factor influences the dose at depth to a significant degree has been shown by Ström and Reinhard (1), who stated that when the thickness of the patient was less than that of the phantom used to establish the depth dose values, the dose at the point of radiation exit was 25 per cent less than the chart values, and that the dose inside

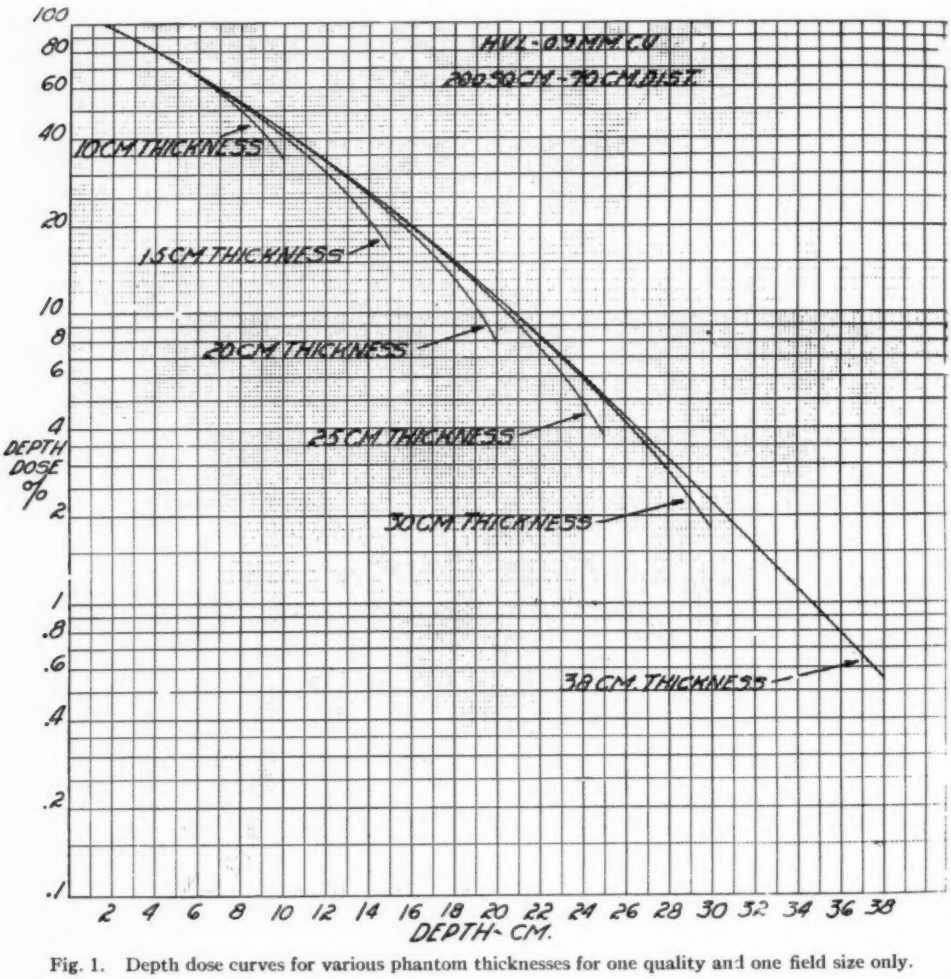

Fig. 1. Depth dose curves for various phantom thicknesses for one quality and one field size only.

[1] From the State Institute for the Study of Malignant Diseases, Buffalo, New York, Dr. William H. Wehr, Acting Director. Accepted for publication in October 1944.

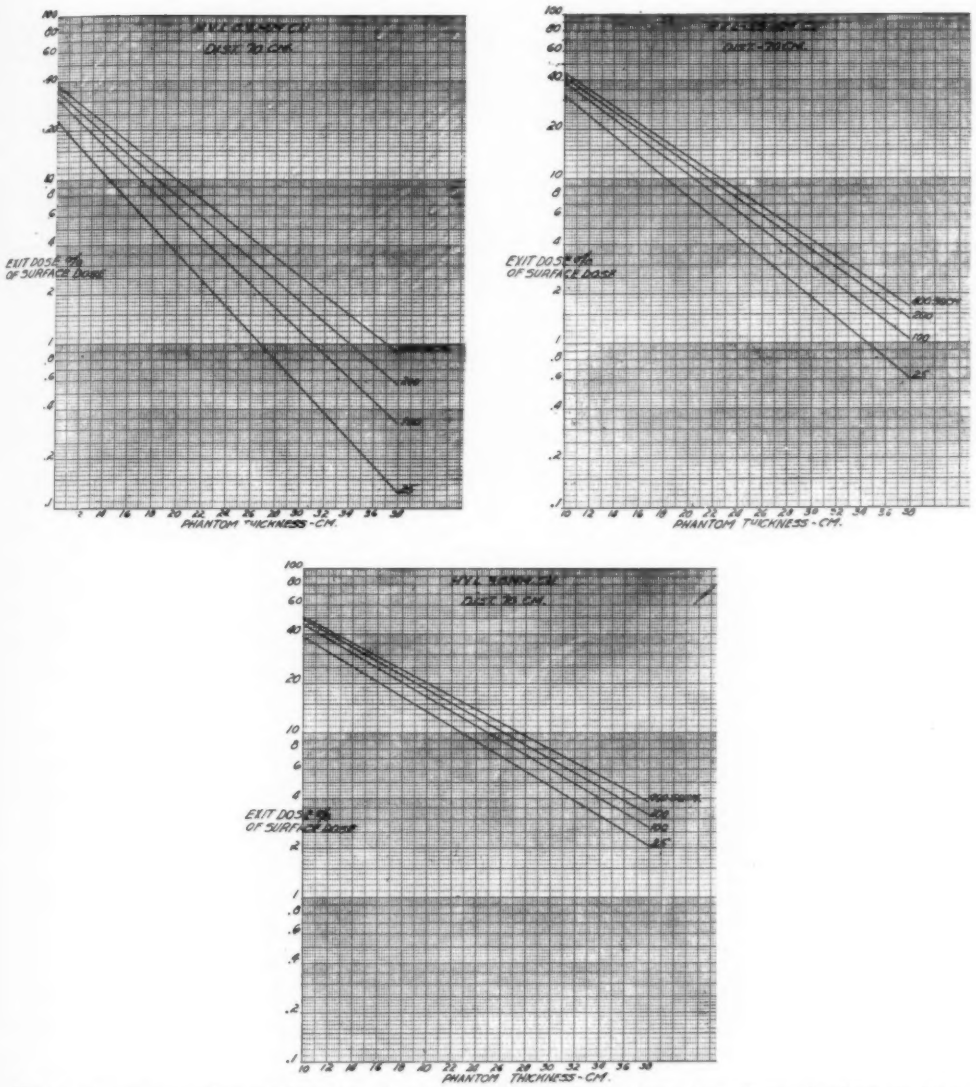

Fig. 2. Curves presenting exit doses for phantom thicknesses ranging from 10 to 38 cm., for three qualities, 0.9, 5.0, 9.0 mm. Cu h.v.l., and for four field sizes.

the tissues near the point of exit would also be somewhat smaller than the chart values. Quimby (2), in her Syllabus of Lectures, also points out that the full phantom depth values at 200 kv. may not be used directly as exit values where the diameter of the irradiated part is smaller than the full phantom thickness. The full phantom values must be reduced by a factor depending on the area treated and on the thickness of the part to be irradiated. The exit doses thus obtained range from 72 to 90 per cent of the full phantom depth values. Aebersold and Chaffee (3) have compared exit doses for 200 kv. with those for 1,000 kv., using four phantom thicknesses. Comparing a 12-cm. phantom with a 24-cm. phantom, they show that the decrease in depth dose associated with the smaller amount of back-scatter of the

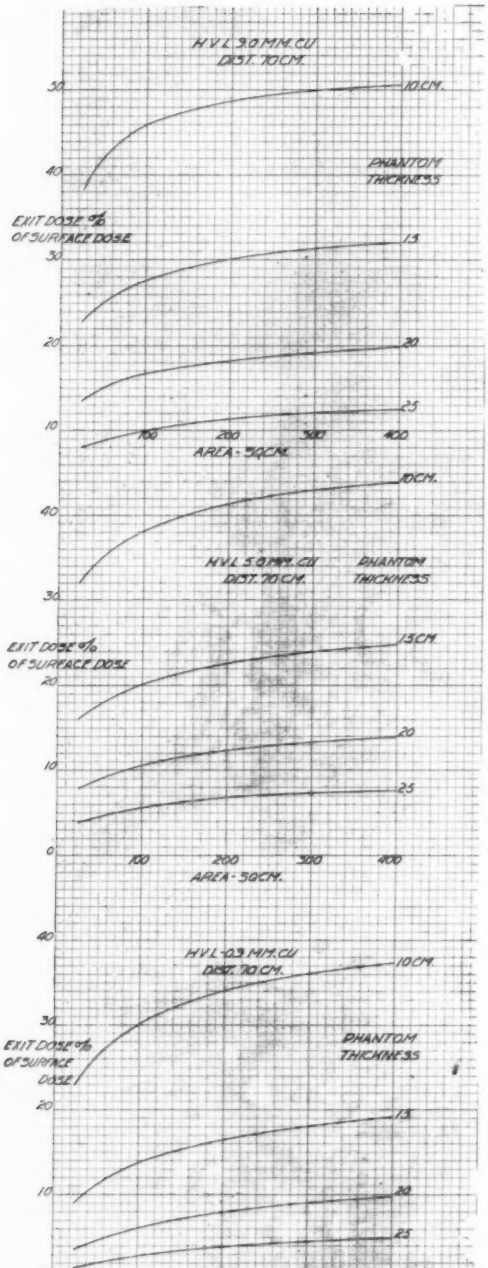

Fig. 3. Curves showing exit doses for field sizes ranging from 25 to 400 sq. cm. for three qualities of radiation and for phantom thicknesses of 10, 15, 20, and 25 cm.

thinner phantom, is apparent approximately 10 cm. above the exit surface.

In order to investigate the relationship between depth dose and exit dose for 200 kv. (0.9 mm. Cu h.v.l.), 400 kv. (5.0 mm. Cu h.v.l.), and 1,000 kv. (9.0 mm. Cu h.v.l.) with field sizes of 25, 100, 200, and 400 sq. cm., measurements were made with a thimble type ionization chamber at 50, 70, and 90 cm. distance. A presdwood phantom[2] was used, whose maximum thickness was 38 cm. This phantom could be divided into sections 10, 15, 20, 25, and 30 cm. thick. The exit surface intensities were determined by one-half submergence of the ionization chamber in a recess in the exit surface of the phantom. In order to simulate conditions which would exist under actual therapy procedure, the phantoms were always resting on a sponge-rubber mattress. The radiation beam was limited by the opening in the tube head and by lead sheets placed directly on the surface of the phantom. These sheets overlapped the surface and had square holes cut in them to give the desired areas. The thicknesses of the lead sheets used for the various voltages were as follows: 1/4 in. for 200 kv., 1/2 in. for 400 kv., and 1 in. for 1,000 kv., in addition to the regular collimating devices.

TABLE I

Phantom Thickness	Reduction
10 cm.	20%
15 cm.	28%
20 cm.	29%
25 cm.	25%
30 cm.	16%

Based on these measurements, families of depth dose curves were drawn for five phantom thicknesses for all quality, area, and distance combinations indicated. A typical family of such curves for one field size and one distance is shown in Figure 1. In this curve the D_5, D_{10}, and D_{15} values for the 38-cm. phantom are the same as those published earlier (4). These curves show that, due to the lack of back-scatter,

[2] This is the same phantom which was used for the measurements published in Radiology **40:** 283–292, March 1943, where, through a typographical error, the thickness was given as 28 cm.

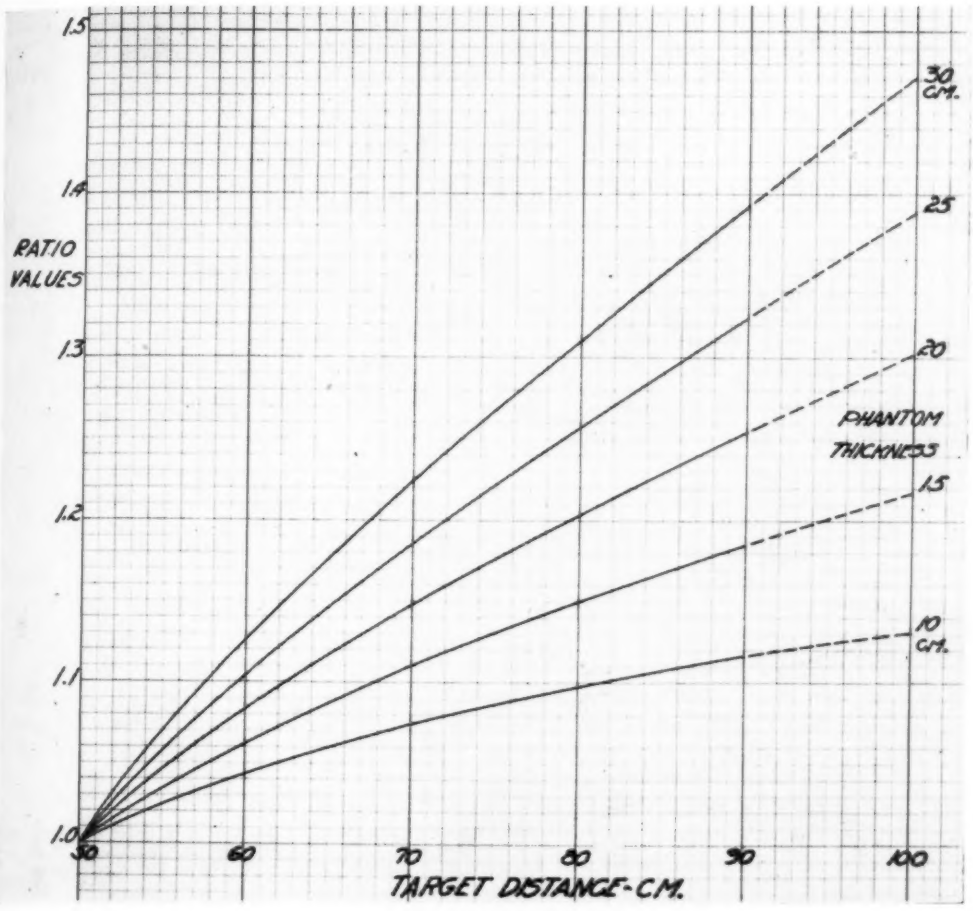

Fig. 4. Distance ratio curves for depth doses at 10, 15, 20, 25, and 30 cm. or exit doses for 10, 15, 20, 25, and 30 cm. phantom thicknesses.

the depth values for any phantom thickness *less than the full phantom* depart from those of the latter at a point 8 to 10 cm. preceding the exit surface. A calculation of the percentage reduction from the full phantom depth values for the various phantom thicknesses is shown in Table I for this particular quality and area only.

The percentage deviation becomes progressively greater with increasing phantom thickness, until the thickness approaches that of the full phantom, when the percentage becomes smaller. However, as pointed out by Quimby (2), the depth dose values for the thicker phantoms are so small that any correction would yield insignificant results. In the previous table, for example, the percentage correction for the 25-cm. phantom is 25 per cent. This would appear to be a large variation, but the depth value for the full phantom at 25 cm. depth is actually only 5.1 per cent, and 25 per cent of 5.1 is insignificant for practical purposes.

It will be noticed, from the family of curves, that a straight line could be drawn through the exit dose values for all of the thicknesses shown in Figure 1. Since the publication of such families of depth curves for all qualities, fields, and distances would occupy too much space, it was decided to limit the published data to the curves

showing only exit values at 70 cm. distance. Figure 2 shows the straight line plot of the exit values for the three qualities and the four areas at 70 cm. distance, when the exit values expressed in terms of per cent of surface dose are plotted on semilog paper against phantom thickness. A plot of the previously published D_5, D_{10}, and D_{15} values, together with the exit dose values for the various phantom thicknesses, would permit complete depth curves to be drawn in a manner similar to Figure 1.

A replot of the data of Figure 2, with exit dose plotted against area, is presented in Figure 3. From these curves it is possible to obtain the exit dose for intermediate areas.

Up to this point we have discussed the exit depth dose relationship for three qualities at 70 cm. distance. By comparing these values with those measured values at 50 and 90 cm. distance, it was found that the exit dose-distance relationship could be expressed in the form of simple ratios for the five phantom thicknesses. These ratios may be applied to all qualities and areas, provided area and quality are constant when transposing from one distance to another. From this series of measurements it was found that these distance ratios, shown in Figure 4, not only apply to exit values but may also be used to calculate depth dose values at 10, 15, 20, 25, and 30 cm. depth.

SUMMARY

A series of curves is presented showing the exit doses for three qualities of radiation, 9.0, 5.0, and 0.9 mm. copper h.v.l., for phantom thicknesses varying from 10 to 38 cm. at 70 cm. distance. Ratio curves are also presented which permit the calculation of exit doses or depth doses for distances from 50 to 90 cm. These exit dose calculations, used in conjunction with previously published depth values, make it possible to derive complete depth dose curves within the limits of field size, distance, and qualities indicated.

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EDITORIAL

Neuroblastoma Sympatheticum

Sympathetic neuroblastoma, with its frequent accompaniment of widespread metastases, has been generally accorded an unfavorable prognosis. From a study of the many accumulated reports, it becomes evident that these tumors are moderately radiosensitive. If they are attacked by radiation therapy or by complete surgical extirpation while still localized at the point of origin, or even after extension to the liver, there is a reasonable chance of permanent cure.

These neoplasms, as their name implies, are classified with the neurogenic tumors, as they originate from the tissue of the sympathetic nervous system in the adrenal medulla or elsewhere. Pepper originally described them as "sarcomas" arising in the adrenals and metastasizing to the liver. Hutchinson later reported primary adrenal tumors with widespread metastases, especially in the skull and bones of the face. It has since been shown that, though they have a special predilection for the skeletal system, metastases may occur in almost any organ of the body and the two types described above are merely different manifestations of the same condition distinguished by the spread of the disease. The areas of spread, however, have a definite implication for the ultimate prognosis, as will be shown later.

Adrenal neuroblastomas are encountered most commonly in children under four years of age but may occur in adults. The initial symptom may be pain referred to the spine and legs, but in most cases an abdominal mass is the primary complaint. Other symptoms depend upon extension of the neoplasm or metastases. One characteristic of the tumor is its tendency to cross the mid-line. Proptosis of one or both eyes with discoloration of the lids may occur in the presence of retro-orbital metastases.

Roentgenograms of the abdomen are not characteristic. With metastases in the long bones, the picture is varied. The most common areas of involvement are in the ends of the diaphyses adjacent to the epiphyseal lines and on the medial border. In advanced cases these changes may extend the full length of the shaft. The resorption may be of uneven density, suggesting a diffuse infiltration rather than massive destruction. There may be osteoporosis of extreme grade before actual destruction takes place. In the skull there is evidence of increased intracranial pressure and a finely granular type of osteoporosis, indicating minute foci of bone resorption. Other flat bones show a similar type of infiltration. The tumor is usually encapsulated and as a rule compresses the kidney rather than invades it. Metastasis to the retroperitoneal lymph nodes is more common than to the bones or liver.

The tumors are quite cellular, with scanty stroma. The cells are small, with hyperchromatic nuclei and a narrow rim of cytoplasm. Rosette formation—a circular arrangement of cells—about bundles of fibrillae is regarded as characteristic of the histologic picture.

For the therapeutic approach, the first consideration is the certainty of a correct diagnosis. In the presence of an abdominal tumor suspected of being a neuroblastoma and with no clinical or roentgen evidence of metastases, an exploratory operation should be undertaken. Complete removal of the tumor should be done if it is free and can be removed without cutting across it. Since the tumors have been shown by a number of observers to be radiosensitive,

postoperative radiotherapy should be given without delay in all cases without known metastases. In those cases with regional extension and peripheral metastases radiotherapy will be found to be of palliative value.

Ladd and Gross (3) report 7 probable cures of abdominal neuroblastoma from a series of 32 histologically verified cases. One patient had been well eight and one-half years with no treatment except biopsy. Three were well seven and one-half, six, and five and one-half years, respectively, following surgical removal without irradiation. Another, with a retroperitoneal growth extending into the spinal canal, was treated by incomplete surgical removal followed by x-ray therapy and was well four years later. Two patients with metastases in the liver received x-ray therapy following operation and biopsy and were in good health after intervals of three and one-half and two years. In view of the rapid course of untreated cases, Ladd and Gross believe that one may speak of a permanent cure if the patient remains well a year after surgical or roentgen therapy. Lehman (4) in 1932 reported a case of surgical removal of a tumor from an infant fifteen years previously. The patient was living and well at the time of the report.

Wyatt and Farber (5), in an extensive review of the subject, include 2 cases with extensive metastases to the liver. Treatment was by x-ray irradiation, and the children were alive and well three and two years later. None of the patients with widespread metastases was cured, although considerable improvement was observed in two. Hauser reported a single case in which metastases in the lungs and cervical lymph nodes disappeared following irradiation. Later, however, generalized metastases led to a fatal termination. In another series (1) of three patients treated by radiation, regression of the local growth was observed in two, but owing to extensive metastases the relief was only temporary. The tumors were moderately radiosensitive.

From the reports cited above it is apparent that, though the prognosis in these cases is without question unfavorable, complete resection or adequate x-ray therapy while the tumor is still localized to the adrenal offers a reasonable chance of complete cure. If the disease has spread to the regional nodes or even metastasized to the liver, there is still a possibility of a favorable outcome, but no report could be found of a cure by any method of treatment after distant metastases had developed.

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AMERICAN BOARD OF RADIOLOGY EXAMINATION

The examination of the American Board of Radiology originally scheduled for June in New York was canceled. The next examination will be in Chicago in the fall. Due notice will be sent out as soon as the time and place have been determined.

NEW ENGLAND ROENTGEN RAY SOCIETY

At its meeting on May 18, 1945, the New England Roentgen Ray Society paid honor to its distinguished member, Dr. George W. Holmes, pioneer radiologist and teacher, by establishing an annual lecture to be known as the George W. Holmes Annual Lecture.

The newly elected officers of the Society are Dr. Philip Batchelder, Providence, R. I., President; Dr. Robert G. Vance, Boston, Vice-President; and Dr. George Levene, Boston, Secretary.

PITTSBURGH ROENTGEN SOCIETY

At a recent meeting of the Pittsburgh Roentgen Society the following officers were elected for the ensuing year: President, Dr. Reuben G. Alley; Vice-President, Dr. Paul Meader; Secretary-Treasurer, Dr. Lester M. J. Freedman.

RADIOLOGICAL SOCIETY OF NEW JERSEY

At the annual meeting of the Radiological Society of New Jersey held on May 16, 1945, the following members were elected to office: President, Dr. H. J. Perlberg, Jersey City; Vice-President, Dr. John Olpp, Englewood; Secretary, Dr. H. R. Brindle, Asbury Park; Treasurer, Dr. W. H. Seward, Orange; Councilor to the American College of Radiology, Dr. J. H. Wyatt, Newark.

DR. CHARLES M. HAMILTON HONORED

Dr. Charles Marshall Hamilton of Nashville, Tenn., a member of the Radiological Society of North America for nearly twenty-five years, was recently chosen president-elect of the Tennessee State Medical Association.

Book Reviews

CLINICAL ROENTGENOLOGY OF THE DIGESTIVE TRACT. By Maurice Feldman, M.D., Assistant Professor of Gastroenterology, University of Maryland; Assistant in Gastroenterology, Mercy Hospital, Baltimore; Consulting Roentgenologist, Sinai Hospital, Baltimore. A volume of 769 pages. Published by The Williams and Wilkins Co., Baltimore. Second Edition, 1945. Price $7.00.

Feldman's "Clinical Roentgenology of the Digestive Tract" was originally published in 1938. This new edition, the second, brings the subject matter satisfyingly up to date. Much of the text has been rewritten and nearly 200 illustrations have been added.

Starting with the esophagus in the first chapter, the author proceeds to discuss the remainder of the digestive tract in orderly, concise, readable, and understandable fashion. All phases of gastro-intestinal roentgenology are adequately, though in some instances briefly, covered. Various diseases and conditions are discussed in clear, direct terms without redundancy, and there are many good suggestions on technic. The bibliography is adequate and, being given immediately following each subject touched upon in a chapter, is easy to find and consult. Special chapters are devoted to the gall-bladder, the pancreas, peritoneum, omentum, the mesentery and retroperitoneal tumors, lymphomatous diseases, the abdominal vessels, the spleen, and deficiency diseases.

The print is easy to read, and the numerous roentgenographic reproductions are of good quality. More illustrations showing gross pathology, would, however, be a useful addition.

The student, the gastroenterologist, and the roentgenologist will find this volume a valuable and ready source of accurate information and a helpful reference work in the study and solution of the multiple and difficult problems encountered in coping with gastro-intestinal tract disease and dysfunction.

WHAT ARE COSMIC RAYS? Revised and Enlarged American Edition. By PIERRE AUGUR, Professor at the Ecole Supérieure Normale, France, Research Associate in Physics, University of Chicago, Fellow of the American Physical Society. Translated from the French by Maurice M. Shapiro. A volume of 128 pages, with numerous photographs. Published by The University of Chicago Press, Chicago. Price $2.00.

The author of "What Are Cosmic Rays?" is an old friend of the radiologists, having worked out and published many of the fundamental discoveries upon which the science of radiology is based. In this book he has done a superb job of writing about cosmic ray research in simple language, directly and accurately—language that any layman can understand, yet free of far-fetched metaphores and misleading analogies. The book is not in any way similar to the manifold "popular science" outbursts so common on the market. The argument is a clever interweaving of history and technic, which works out in a most entertaining manner.

Since a critic must criticize something, it might

RALPH EMERSON MYERS
1888-1945

be said that the author should have done a better job of showing the practical value of his work. Cosmic ray research has made it possible to understand and apply the power that has come to us through the newer developments of high-voltage generators and radioactive substances. The author begins by telling about the early discoveries and, at the same time, the instruments that made these discoveries possible, giving a completely interwoven account of events as they actually happened. People who have had no occasion to work with a Geiger counter or study the complexities of a cloud chamber may obtain a painless understanding of these things in the first ten pages, enough so that they can enjoy the rest of the story as it unfolds.

The second chapter deals with cosmic ray exploration. It avoids all the pitfalls which might have made it a boring tale of adventure and explains why and how the cosmic-ray map of the world was plotted and intensity measurements were made in the stratosphere and the depth of the ocean. From there on the book deals with the energetic particles that are components of the cosmic ray, their nature and behavior, and what is known of their significance. The reader is offered a first-class literary acquaintance with the mesotron and its relatives. In the end he is brought up to date, as nearly as possible, and given food for thought as to future developments.

MASS RADIOGRAPHY OF THE CHEST. By HERMAN E. HILLEBOE, M.D., Medical Director, Chief, Tuberculosis Control Division, U. S. Public Health Service; Professorial Lecturer on Tuberculosis Control, George Washington University School of Medicine, Washington, D. C., and RUSSELL H. MORGAN, M.D., Surgeon (R), Medical Officer-in-Charge, Radiology Section, Tuberculosis Control Division, U. S. Public Health Service; Assistant Professor of Roentgenology (absent on leave), The University of Chicago. A volume of 288 pages, with 93 illustrations. Published by the Year Book Publishers, Inc., Chicago, Ill. Price $3.50.

This small manual is a much needed volume giving a well rounded picture of mass radiography of the chest. Every phase of the subject is covered with clarity and in sufficient detail for practical purposes. The authors set forth the methods of applying the procedure to industrial surveys, surveys of the civilian population, and to general hospital work, discussing such projects from the standpoint of space requirements, personnel, apparatus, and the rapid handling of patients.

The description of the various types of available equipment is valuable and informative. The chapter on physical factors affecting the choice of equipment includes much new material on x-ray physics, especially as applied to photofluorography. The roentgen technic is described and special emphasis is placed on protection of the operator.

The chapter on roentgen diagnosis is concise and presents clearly the important changes that may be discovered in a study of miniature films. It is illustrated with 48 full-page photofluorograms.

The book is attractively printed and illustrated and is especially timely now that new equipment for mass surveys may soon become available. It should be in the possession of every roentgenologist, as well as those interested in tuberculosis and industrial medicine.

In Memoriam

RALPH EMERSON MYERS, M.D.

1888–1945

Dr. Ralph Emerson Myers of Oklahoma City, Counselor of the Radiological Society of North America for his state, died after a brief illness on March 14, 1945. Dr. Myers was born in Buskirk, New York, in 1888. He was graduated from Yale University in 1909 and received his master's degree the following year. He was chief chemist at the Battle Creek Sanitarium in 1910–11, held the Austin teaching fellowship in physiology at the Harvard Medical School in 1911–12, and was successively lecturer (1912–13) and adjunct professor (1913–14) of pharmacology and physiology in Albany Medical College (Union University). He received his M.D. from Cornell Medical College in 1918 and served his internship in Memorial Hospital, New York. After a year's service in the Army, he returned to teaching, first as professor of pharmacology in the University of Maryland School of Medicine (1919–20) and then of pharmacology and physiological chemistry in the George Washington University School of Medicine (1920–22). He was director of laboratories in St. Anthony's Hospital, Oklahoma City, from 1920 to 1929, after which date he devoted himself to practice in that city.

Dr. Myers was a fellow of the American Medical Association and of the American College of Radiology. He was a diplomate of the American Board of Radiology and a member of the American Radium Society and of the Radiological Society of North America, as well as of the American Society of Clinical Pathologists, the American Society for the Study of Neoplastic Diseases, the American Association for the Advancement of Science, and the Southern Medical Association.

WILLIAM MARSHALL BARRON

1890–1945

Dr. Wm. Marshall Barron of Ackerman, Miss., died on Jan. 18, 1945. Doctor Barron received his medical degree from Tulane University in 1914 and practised in San Antonio, Texas, where he was roentgenologist to the Robert B. Green Memorial Hospital. He was a member of the Radiological Society of North America.

RADIOLOGICAL SOCIETIES OF NORTH AMERICA

Editor's Note.—Will secretaries of societies please cooperate by sending information to Howard P. Doub, M.D., Editor, Henry Ford Hospital, Detroit 2, Mich.

UNITED STATES

Radiological Society of North America.—Secretary, D. S. Childs, M.D., 607 Medical Arts Bldg., Syracuse 2, N.Y.

American Roentgen Ray Society.—Secretary, Harold Dabney Kerr, M.D., Iowa City, Iowa.

American College of Radiology.—Secretary, Mac F. Cahal, 20 N. Wacker Dr., Chicago 6, Ill.

Section on Radiology, American Medical Association.—Secretary, U. V. Portmann, M.D., Cleveland Clinic, Cleveland 6, Ohio.

ARKANSAS

Arkansas Radiological Society.—Secretary, J. S. Wilson, M.D., Monticello. Meets every three months and annually at meeting of State Medical Society.

CALIFORNIA

California Medical Association, Section on Radiology.—Secretary, Gordon King, M.D., Children's Hospital, San Francisco.

Los Angeles County Medical Association, Radiological Section.—Secretary, Roy W. Johnson, M.D., 1407 South Hope St., Los Angeles. Meets second Wednesday of each month at County Society Building.

Pacific Roentgen Society.—Acting Secretary, Frederick H. Rodenbaugh, M.D., 490 Post St., San Francisco. Meets annually with California Medical Association.

San Diego Roentgen Society.—Secretary, Henry L. Jaffe, M.D., U. S. Naval Hospital, San Diego, Calif. Meets first Wednesday of each month.

San Francisco Radiological Society.—Secretary, Carlton L. Ould, University Hospital, Medical Center, San Francisco 22. Meets monthly on the third Thursday at 7:45 P.M., first six months of the year in Lane Hall, Stanford University Hospital, and second six months in Toland Hall, University of California Hospital.

COLORADO

Denver Radiological Club.—Secretary, A. Page Jackson, Jr., M.D., 304 Republic Bldg., Denver 2. Meetings third Friday of each month, Denver Athletic Club.

CONNECTICUT

Connecticut State Medical Society, Section on Radiology.—Secretary, Max Climan, M.D., 242 Trumbull St., Hartford 3. Meetings bimonthly, second Thursday.

FLORIDA

Florida Radiological Society.—Secretary-Treasurer, J. F. Pittman, M.D., Blanche Hotel Annex, Lake City.

GEORGIA

Georgia Radiological Society.—Secretary-Treasurer, James J. Clark, M.D., 478 Peachtree St., N. E., Atlanta 3. Meets in November and at the annual meeting of State Medical Association.

ILLINOIS

Chicago Roentgen Society.—Secretary, Fay H. Squire, M.D., 1753 W. Congress St., Chicago 12. Meets at the Palmer House, second Thursday of October, November, January, February, March, and April.

Illinois Radiological Society.—Secretary-Treasurer, William DeHollander, M.D., St. Johns' Hospital, Springfield. Meetings quarterly by announcement.

Illinois State Medical Society, Section on Radiology.—Secretary, Frank S. Hussey, M.D., 250 East Superior St., Chicago 11.

INDIANA

The Indiana Roentgen Society.—Secretary-Treasurer, Harold C. Ochsner, M.D., Methodist Hospital, Indianapolis 7. Annual meeting in May.

IOWA

The Iowa X-ray Club.—Secretary, Arthur W. Erskine, M.D., Suite 326 Higley Building, Iowa City. Holds luncheon and business meeting during annual session of Iowa State Medical Society.

KENTUCKY

Kentucky Radiological Society.—Secretary-Treasurer, Sydney E. Johnson, 101 W. Chestnut St., Louisville.

LOUISIANA

Louisiana Radiological Society.—Secretary-Treasurer, Johnson R. Anderson, M.D., North Louisiana Sanitarium, Shreveport. Meets annually at same time as State Medical Society.

Shreveport Radiological Club.—Secretary, Oscar O. Jones, M.D., 2622 Greenwood Road. Meets monthly September to May, third Wednesday, 7:30 P.M.

MARYLAND

Baltimore City Medical Society, Radiological Section.—Secretary, Charles N. Davidson, M.D., 101 West Read St., Baltimore 1.

MICHIGAN

Detroit X-ray and Radium Society.—Secretary-Treasurer, E. R. Witwer, M.D., Harper Hospital, Detroit 1. Meetings first Thursday of each month from October to May, at Wayne County Medical Society club rooms.

Michigan Association of Roentgenologists.—Secretary, Bruce MacDuff, M.D., 201 Sherman Bldg., Flint 3.

MINNESOTA

Minnesota Radiological Society.—Secretary, A. T. Stenstrom, M.D., Minneapolis General Hospital, Minneapolis 26. Meetings quarterly.

MISSOURI

Radiological Society of Greater Kansas City.—Secretary, John W. Walker, M.D., 306 E. 12th St., Kansas City, Mo. Meetings last Friday of each month.

St. Louis Society of Radiologists.—Secretary, Edwin C. Ernst, M.D., 100 Beaumont Medical Bldg. Meets on fourth Wednesday of each month except June, July, August, and September.

NEBRASKA

Nebraska Radiological Society.—Secretary-Treasurer, Donald H. Breit, M.D., University of Nebraska Hospital, Omaha 5. Meetings third Wednesday of each month at 6 P.M. in either Omaha or Lincoln.

NEW ENGLAND

New England Roentgen Ray Society.—Secretary-Treasurer, George Levene, M.D., Massachusetts Memorial Hos-

pitals, Boston, Mass. Meets monthly on third Friday at Boston Medical Library.

NEW HAMPSHIRE

New Hampshire Roentgen Society.—Secretary-Treasurer, Richard C. Batt, M.D., St. Louis Hospital, Berlin.

NEW JERSEY

Radiological Society of New Jersey.—Secretary, H. R Brindle, M.D., 501 Grand Ave., Asbury Park. Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called.

NEW YORK

Associated Radiologists of New York, Inc.—Secretary, William J. Francis, M.D., East Rockaway, L. I.

Brooklyn Roentgen Ray Society.—Secretary-Treasurer, Leo A. Harrington, M.D., 880 Ocean Ave., Brooklyn 26. Meets fourth Tuesday of every month, October to April.

Buffalo Radiological Society.—Secretary-Treasurer, Joseph S. Gian Franceschi, M.D., 610 Niagara St., Buffalo 1. Meetings second Monday evening each month, October to May, inclusive.

Central New York Roentgen Society.—Secretary-Treasurer, Carlton F. Potter, M.D., 425 Waverly Ave., Syracuse 10. Meetings in January, May, and October.

Long Island Radiological Society.—Secretary, Marcus Wiener, M.D., 1430 48th St., Brooklyn 19. Meetings fourth Thursday evening each month at Kings County Medical Bldg.

New York Roentgen Society.—Secretary, Wm. Snow, M.D., 941 Park Ave., New York 28.

Rochester Roentgen-Ray Society.—Secretary, Murray P. George, M.D., 260 Crittenden Blvd., Rochester 7. Meets at Strong Memorial Hospital, third Monday, September through May.

NORTH CAROLINA

Radiological Society of North Carolina.—Secretary-Treasurer, Major I. Fleming, M.D., 404 Falls Road, Rocky Mount. Meets in May, and October.

NORTH DAKOTA

North Dakota Radiological Society.—Secretary, Charles Heilman, M.D., 1338 Second St., N., Fargo.

OHIO

Ohio Radiological Society.—Secretary, Henry Snow, M.D., 1061 Reibold Bldg., Dayton 2. Next meeting at annual meeting of the Ohio State Medical Association.

Cleveland Radiological Society.—Secretary-Treasurer, Don D. Brannan, M.D., 11311 Shaker Blvd., Cleveland 4. Meetings at 6:30 P.M. on fourth Monday of each month from October to April, inclusive.

Radiological Society of the Academy of Medicine (Cincinnati Roentgenologists).—*Secretary-Treasurer,* Samuel Brown, M.D., 707 Race St., Cincinnati 2. Meetings held third Tuesday of each month.

PENNSYLVANIA

Pennsylvania Radiological Society.—Secretary-Treasurer, L. E. Wurster, M.D., 416 Pine St., Williamsport 8. The Society meets annually.

Philadelphia Roentgen Ray Society.—Secretary, Calvin L. Stewart, M.D., Jefferson Hospital, Philadelphia 7. Meets first Thursday of each month at 8:00 P.M., from October to May, in Thomson Hall, College of Physicians, 21 S. 22d St.

Pittsburgh Roentgen Society.—Secretary-Treasurer, Lester M. J. Freedman, M.D., 4800 Friendship Ave., Pittsburgh 24. Meets second Wednesday of each month at 6:30 P.M., October to May, inclusive, at The Ruskin, 120 Ruskin Ave.

ROCKY MOUNTAIN STATES

Rocky Mountain Radiological Society (North Dakota, South Dakota, Nebraska, Kansas, Texas, Wyoming, Montana, Colorado, Idaho, Utah, New Mexico).—*Secretary,* A. M. Popma, M.D., 220 North First St., Boise, Idaho.

SOUTH CAROLINA

South Carolina X-ray Society.—Secretary-Treasurer, Robert B. Taft, M.D., 103 Rutledge Ave., Charleston 16.

TENNESSEE

Memphis Roentgen Club.—Chairmanship rotates monthly in alphabetical order. Meetings second Tuesday of each month at University Center.

Tennessee Radiological Society.—Secretary-Treasurer, J. Marsh Frère, M.D., 707 Walnut St., Chattanooga. Meeting annually with State Medical Society in April.

TEXAS

Dallas-Fort Worth Roentgen Study Club.—Secretary, X. R. Hyde, M.D., Medical Arts Bldg., Fort Worth, Texas. Meetings on third Monday of each month, in Dallas in the odd months and in Fort Worth in the even months.

Texas Radiological Society.—Secretary-Treasurer, Asa E. Seeds, M.D., Baylor Hospital, Dallas.

VIRGINIA

Virginia Radiological Society.—Secretary, E. Latané Flanagan, M.D., 215 Medical Arts Bldg., Richmond 19.

WASHINGTON

Washington State Radiological Society.—Secretary-Treasurer, Thomas Carlile, M.D., 1115 Terry Ave., Seattle. Meetings fourth Monday of each month, October through May, at College Club, Seattle.

WISCONSIN

Milwaukee Roentgen Ray Society.—Secretary-Treasurer, C. A. H. Fortier, M.D., 231 W. Wisconsin Ave., Milwaukee 3. Meets monthly on second Monday at the University Club.

Radiological Section of the Wisconsin State Medical Society.—Secretary, S. R. Beatty, M.D., 185 Hazel St., Oshkosh. Two-day annual meeting in May and one day in connection with annual meeting of State Medical Society in September.

University of Wisconsin Radiological Conference.—Secretary, E. A. Pohle, M.D., 414 N. Charter St., Madison 6. Meets first and third Thursdays, 4 to 5 P.M., September to May, inclusive, Room 301, Service Memorial Institute.

CANADA

Canadian Association of Radiologists.—Honorary Secretary-Treasurer, J. W. McKay, M.D., 1620 Cedar Ave., Montreal.

La Société Canadienne-Française d'Electrologie et de Radiologie Médicales.—General Secretary, Origène Dufresne, M.D., Institut du Radium, Montreal. Meets on third Saturday of each month.

CUBA

Sociedad de Radiología y Fisioterapia de Cuba.—Offices in Hospital Mercedes, Havana. Meets monthly.

ABSTRACTS OF CURRENT LITERATURE

ROENTGEN DIAGNOSIS

The Head and Neck

The Chest

The Digestive System

The Suprarenals

The Skeletal System

Gynecology and Obstetrics

The Genito-Urinary System

The Blood Vessels

Endocrinology

Foreign Bodies

RADIOTHERAPY

Neoplasms

Non-Neoplastic Diseases

Radiation Effects

Among the abstracts in this issue are some from Acta Radiologica for 1942, issues of that journal for the War years having just become available. While it is the policy of Radiology, so far as possible, to abstract papers within nine or ten months, at most, of their original publication, it has seemed worth while to bring to our readers this somewhat older material which might not otherwise come to their attention. More abstracts from this important radiological publication will appear in forthcoming issues. It is hoped that other foreign journals, also, may soon be represented in these pages.

ROENTGEN DIAGNOSIS

THE HEAD AND NECK

Metabolic Craniopathy: Clinical and Roentgenologic Study of So-Called Hyperostosis Frontalis Interna. A. Grollman and J. P. Rousseau. J. A. M. A. **126:** 213–217, Sept. 23, 1944.

Metabolic craniopathy has been defined as a "syndrome characterized clinically by variable and protean manifestations of a metabolic, endocrine, and neuropsychiatric nature, and roentgenologically by characteristic thickening of the internal tables of the skull." The more frequent designation, "hyperostosis frontalis interna," is open to the objections that the changes in the skull are not always limited to the frontal bones; that they do not appear to contribute to the clinical picture, nor are they probably an essential part of the syndrome, though they still remain the most characteristic feature of the disorder.

Stewart (J. Neurol. & Psychopath. **8:** 321, 1928) was the first to describe this entity, reporting 5 cases. The present authors found calvarial hyperostosis, indicative of metabolic craniopathy, in 78 of 1,620 skull examinations (4.1 per cent) made between July 1941 and January 1944. The clinical data here presented are based on 40 of these cases and on 2 without x-ray evidence of hyperostosis.

Females in the fifth decade are most commonly affected, but the youngest patient in the authors' series was twenty-one. Only one male was observed. In a number of instances the history suggested an hereditary factor.

In 14 of the patients there was a combination of neuropsychiatric, metabolic, and endocrine symptoms; in 13 neuropsychiatric manifestations were outstanding; in 8 neuropsychiatric and metabolic complaints predominated; in 5 neuropsychiatric and endocrine difficulties were most marked, and in 2 the changes in the skull were observed before questioning elicited the neuropsychiatric difficulty.

Obesity, amenorrhea, hirsutism, hypertension, and extremely variable neuropsychiatric difficulties were the common findings. The characteristic roentgen observation was the deposition of cancellous bone of great density on the inner table of the frontal bone in a relatively symmetrical fashion. This formation consists of benign non-inflammatory osseous tissue, affecting primarily the compact bone of the inner table. In a small percentage of cases it later involves the diploe between the tables. In the majority of the cases the lesion is entirely limited to the squama frontalis, the condition which is recognized as typical hyperostosis frontalis interna. Occasionally there is involvement of the orbital plate of the frontal bone, the inner table of the parietal bone or, less commonly, the structures in the middle fossa at the base of the skull, especially the temporal or sphenoid bone and the bony structures of the hypophyseal fossa. Diffuse calvarial hyperostosis involving the entire vault and extracalvarial bone changes in the mandible have been reported. In none of the authors' cases were changes demonstrated outside the calvarium.

Metabolic craniopathy is differentiated from Cushing's syndrome by slow progression and absence of osteopetrosis, acrocyanosis, and purplish striae. The 17-ketosteroid excretion, which is of considerable significance in Cushing's syndrome and adrenal cortex disorders, is within normal limits.

No form of treatment led to permanent benefit. Irradiation of the pituitary and hypothalamic areas produced striking improvement in several patients but others showed no apparent benefit.

ROBERT S. MACINTYRE, M.D.
(University of Michigan)

Roentgenographic Evidence of Relief of Chronic Increased Intracranial Pressure Following a Torkildsen Operation. Eric Oldberg. Arch. Neurol. & Psychiat. **52:** 230–232, September 1944.

The Torkildsen operation consists of by-passing an obstructed sylvian aqueduct by connecting a lateral ventricle and the cisterna magna with a rubber catheter. The purpose is to overcome chronic increased intracranial pressure.

That the Torkildsen procedure is efficacious is spectacularly illustrated by a case recorded by Oldberg. The operation was done on a nineteen-year-old girl with atresia aqueducti, who presented characteristic roentgen signs of increased intracranial pressure, *viz.*, erosion of the sella turcica, spreading of the cranial sutures, and increase in prominence of the digital markings on the inner table of the cranial vault. After two years of symptomatic relief of pressure, roentgenograms showed very obvious recalcification and obliteration of the pressure markings, increase in the thickness of the skull, increased contrast of the frontal sinuses, and diminution in size of the formerly expanded and thinned sella turcica.

JOHN F. HOLT, M.D.
(University of Michigan)

Torular Granuloma Simulating Cerebral Tumor. H. S. Swanson and W. A. Smith. Arch. Neurol. & Psychiat. **51:** 426–431, May 1944.

Although meningitis is the common manifestation of torula infection in the brain, a large granuloma occasionally occurs, giving a clinical picture of intracranial neoplasm. Two such cases are reported in this article.

In typical instances of torular meningitis, the causative organisms can be grown with ease from the spinal fluid, and at times from the blood, urine, and sputum as well. On the other hand, intracranial torular granulomas may occur without yielding such conclusive bacteriological findings. Thus, the preoperative diagnosis may be extremely difficult.

Since *T. histolytica* frequently involves the lungs, the authors advocate routine roentgenographic examination of the chest in all cases in which cerebral tumor is suspected. Such procedure may occasionally give an important diagnostic clue to torular infection, as well as to the presence of primary pulmonary neoplasm, which is notorious for the production of cerebral metastases.

Roentgenograms of the skull were made in both of the patients reported, but there is no record of intracranial pneumography having been done. Actually such procedure might prove to be extremely confusing, since one of the patients had three separate granulomas.

JOHN F. HOLT, M.D.
(University of Michigan)

Pharyngo-Esophageal Diverticula. Max M. Kulvin. Illinois M. J. **86:** 198–205, October 1944.

Pharyngo-esophageal diverticula may be caused by loss of elasticity or degeneration of the muscles composing the lower pharyngeal constrictors, or by persistence of contraction of the sphincteric portion of the cricopharyngeus muscle during deglutition.

Five cases are presented. All of these patients did not have the same complaints, some stressing some things more than others. The "composite" symptoms were: (1) pain in the throat or below, with a "catching" sensation after swallowing, (2) coughing up of food particles, (3) sensation of belching during talking, when pressure is made over one side of the neck or the other, (4) fullness in the neck after eating, (5) difficulty in clearing the throat, (6) occasional difficulty in taking liquids, (7) loss of weight despite good appetite. Hoarseness due to pressure on the recurrent laryngeal nerve and ptosis or exophthalmos due to pressure on the cervical sympathetic plexus may occur.

Diagnosis is based on the symptoms and roentgenographic and fluoroscopic findings. Usually nothing is found on physical examination. Rarely there is a ballooning out of the lower part of the neck on swallowing. Pharyngo-esophageal diverticula must be differentiated from carcinoma of the hypopharynx and upper esophagus and from esophageal stenosis, hysteria, and acute and chronic infections. Esophagoscopy is of aid in determining the presence of a tumor or stenosis.

The treatment of pharyngo-esophageal diverticula is surgical except in the very old patient. The author favors the one-stage operation.

Fractures of the Zygomatic Tripod. H. Gordon Ungley and Stephen C. Suggit. Brit. J. Surg. **32:** 287–299, October 1944.

Fourteen cases of fracture of the zygomatic tripod are reported in detail. The injuries were severe, occurring mostly in members of the Armed Forces. Roentgenograms accompany most of the case reports but these do not show very clearly the fractures described in the text.

The injury was on the left side in 10 cases and on the right in 4. Two patients had complicating fractures of other bones, including a fracture of the skull with paralysis of the 6th and 7th cranial nerves. Diplopia occurred in 4 cases and infra-orbital nerve involvement in 3 cases. In one case there was comminution of the antral wall and a cartilage graft was used to cover the deficiency. Infection followed, necessitating the removal of the graft, and the space in the antrum was wired. Operation was performed by the canine fossa route in 4 cases and by the temporal route in 5 cases. The end-results were good in 7 cases. In one case there was residual separation of the zygomaticofrontal articulation, and in another case there was considerable residual deformity.

The clinical features of these fractures are facial deformity, flattening of facial contour, and a palpable fracture line along the orbital margin. Infra-orbital nerve injury with anesthesia or pain occurred in 7 of the 14 cases. Hemorrhage into the maxillary antrum is a fairly common complication.

For roentgen examination the most useful view is the mentonasal, such as is used to demonstrate the maxillary antra. The main points to note in the region of the maxillary antrum are the degree of comminution of the anterior wall of the antrum, the degree of impaction and telescoping of the zygoma into the cavity of the antrum, and the associated antral opacity. The usual views are not of much help in determining the degree of comminution of the antral wall. For this purpose, the following technic, proposed by Dr. Graham Hodgson, proved useful. The head is placed in the occipito-mental position, *i.e.*, the chin resting against the Potter-Bucky and the orbital-mental line at an angle of 45 degrees to the horizontal, this angle being open toward the feet with the patient in the erect posture. The head is then tilted over toward the opposite or intact side, and at the same time the face is slightly rotated toward that side, approximately 10 to 15 degrees. In this position the fractures are shown as clear-cut lines. There is always some opacity in the antrum, due either to hemorrhage into the cavity or to edema of the lining mucosa. The presence of a fluid level is positive evidence of hemorrhage.

Another point to be considered in the roentgen examination is separation and/or fracture in the region of the zygomatic-frontal synostosis. This occurred in 50 per cent of the cases in this series. Separation can occur without fracture. Separation and/or fracture in the region of the zygomatic-temporal synostosis is also of significance, as this increases the mobility of the zygoma. It occurred in 5 cases of this series.

Fractures of the zygomatic-maxillary arch result from direct injury but the type of fracture varies with direction and site of the blow. A blow from the anterolateral aspect, the most common cause, results in the zygoma as a whole being driven posteriorly and medially into the antrum. There is often comminution of the maxilla and of the zygoma. Separation of the synostosis between the zygomatic and frontal, and between the zygomatic and temporal bones is common in this group. Frontal blows produce a double vertical fracture line—one through the anterior antral wall and the other through the body of the zygoma—the intervening block of bone being forced directly backward. With blows from the nasal or anteromedial aspect, the anterolateral portion of the maxilla, together with the zygoma, is forced backward and laterally, carrying a large part of the orbital floor and infra-orbital margin in the same direction.

Early diagnosis and treatment are very important to prevent facial disfigurement and complications. Reduction may be done by the temporal route or the canine fossa approach. Wiring of the zygomatic-frontal articulation was used in a few cases with wide separation and where a deficiency in the antral wall occurred.

MAX CLIMAN, M.D.

THE CHEST

Indispensability of Routine X-Ray Examinations of the Chest in a General Clinic. Robert G. Bloch and William B. Tucker. Am. Rev. Tuberc. **50:** 405–417, November 1944.

Routine fluoroscopic examination of the chests of all patients has been adopted as a standard procedure at the University of Chicago Clinics, and the results obtained from the first 15,000 patients are presented. Of this number, 4.17 per cent were found to have tuberculous lesions of the reinfection type, with the disease considered clinically important in 1.43 per cent. In addition, a large number of other pulmonary and car-

diac lesions were observed, the most important being malignant neoplasms, with an incidence of 0.6 per cent, and cardiovascular disease, seen in 14.4 per cent of those examined. Fluoroscopy precedes clinical examination, and the fluoroscopic report is immediately available to the examining physician. This is one advantage of fluoroscopy over film methods in a large general clinic. L. W. PAUL, M.D.

Intrathoracic Metallic Foreign Bodies. A. L. d'Abreu, J. W. Litchfield, and C. J. Hodson. Lancet **2:** 265–268, Aug. 26, 1944.

In a group of 264 patients with severe chest wounds, seen at a forward general hospital within two to fifty days of the injury, there were 92 with retained intrathoracic missiles (excluding shell fragments or bullets superficial to the rib plane). Because of the danger of infection, hemorrhage, and structural damage, it has been the authors' practice to remove fragments measuring 1 cm. or more unless the anatomical approach involves too great a risk. Of the 50 patients in this series operated upon, 48 made a good recovery. Foreign bodies were removed from the lung in 25 cases, with one death; from the pleural cavity in 14; from the mediastinum or pericardium in 7; and from the endothoracic fascia in 4. One retained intracardiac missile lay in the interventricular septum and was not removed; the patient died. The most common complication on admission was pleural infection; 10 patients, subsequently operated upon for removal of the missile, arrived with this condition established. Lung abscess was seen in 5 cases; 2 of these patients died from secondary hemorrhage without operation.

Roentgenography plays an important part in assessing the suitability of patients for operation. It assists in determining the exact anatomical location and size of the foreign body, the state of the pleura and lung, and the amount of damage along the track of the missile. Posterio-anterior and lateral films are first taken, using deep penetration if necessary because of effusion, lung contusion, or atelectasis. For intrapulmonary missiles these views usually suffice, and the exact position of the missile in relation to heart, hilum, or lobes of the lung can be determined. It is especially useful to know whether the fragment lies near a fissure and to which lobal surface it seems closest.

For investigation of metal fragments lying close to the chest wall, the diaphragm, or heart, fluoroscopy is the method of choice. The underlying principle is so to position the patient that the central ray of the x-ray beam passes tangentially to the parietes at the site of the foreign body. Only thus can it be determined whether the missile lies within or without the chest. The same holds good for the diaphragm, and a tube that can be angulated tangentially to the dome of the diaphragm is invaluable in determining the position of missiles relative to it. In the region of the paravertebral gutter, it may be impossible, owing to the thickness of tissue, to say definitely where the missile lies, but enough information can be provided to enable the surgeon to proceed with exactness.

Estimated distances from the mid-line and the rib level, posteriorly or anteriorly, are helpful. When missiles lie in, or just outside, the rib plane, they are located with a needle under the fluoroscopic screen before operation. Only if paracardiac foreign bodies cannot be separated from the heart outline by a thorough all-round-heart tangential screening is it safe to assume their presence within the pericardium or heart wall. Very small intracardiac foreign bodies were twice missed on the film (because their movement blurs the shadows they cast) and were revealed only on fluoroscopy.

Roentgenography should give the surgeon an accurate account of the difficulties he is likely to meet. Rib damage, effusion, pleural fibrin deposit, collapse, lung contusion, missile track, the proximity of bronchi or calcified nodes (easily mistaken for foreign bodies at operation) are the most important conditions to assess. For example, the presence of strong adhesions or a tough "missile track" may necessitate an entirely different method of approach. On the other hand, localization of the foreign body at operation may be greatly facilitated by finding a "track" leading down to it. Again, when a lobe collapses, the position of a foreign body in it may be altered by a matter of inches.

By careful study of the course of the missile from its entry to its position of rest, the damage may be estimated with fair accuracy. Thoracotomy is often used for repairing injury to rib or diaphragm, as well as for removal of the foreign body.

In 4 cases, the foreign body was not easily found at operation. In these cases, fluoroscopy was done in the operating room and the foreign body localized by means of parallax and an opaque instrument or by passing a needle down to it.

The approach chosen for removal of missiles in the lungs depends largely on the roentgen findings and the state of the pleura. Classical thoracotomy, anterior thoracotomy, subcapsular thoracotomy, and a small intercostal incision have been employed. After removal of lung missiles the pleural cavity is not drained unless infection was present before operation.

Missiles lodging in the endothoracic fascia may give rise to an extrapleural hemothorax. This condition has occurred eleven times in this series. It is commonly associated with fracture of ribs by missiles with or without pleural penetration. An effusion as large as ten to twenty ounces may be present. Roentgenological characteristics of extrapleural hemothorax are: The effusion is almost always localized to a part of the chest wall, without spreading diffusely up or down it. It may arise gently or steeply at its periphery. In 2 of the authors' cases it appeared "overhanging" at its lower edge. It may indent the lung for several centimeters. When viewed at right angles to the plane of its base, it appears as a diffuse shadow, but in the late stages it may have a well defined border. It usually casts a dense shadow and may be accompanied by an intrapleural effusion. When situated in the region of the apex it has a tendency to lie over it like a cap. In size it may vary from a small "blister" to a large rounded collection 15 cm. across its base. There is almost always damage to adjacent ribs.

Many of the 264 cases forming the basis of this paper are included in the series of 260 "major complications of penetrating wounds of the chest" analyzed by the same authors in an earlier issue of the Lancet (**2:** 197 Aug. 12, 1944).

Primary Atypical Pneumonia. Report of Forty-Seven Cases. Don W. Chapman. J. Iowa M. Soc. **34:** 391–395, September 1944.

Forty-seven cases of atypical pneumonia are analyzed, the data being presented in the form of a table.

The author's observations are similar to those reported by others.

Roentgen Aspect of Atypical or Virus Pneumonia. Russell W. Bernhard. J. Iowa M. Soc. **34:** 395–402, September 1944.

Six cases of atypical pneumonia are reported, each illustrated by several successive roentgenograms. In one of these cases roentgen therapy was given—three doses of 100 r (200 kv., Thoraeus filter, h.v.l. equivalent to 1.95 mm. Cu) to the anterior chest, on successive days. The patient, who had been extremely ill, showed an excellent response.

Atypical Pneumonia: A Diagnostic Problem in the Tropics. Philip A. Tumulty. Bull. Johns Hopkins Hosp. **75:** 269–302, November 1944.

Ninety-three cases of atypical pneumonia seen in a U. S. Army General Hospital on an island of the Fiji group from Oct. 1, 1942, to April 1, 1944, are analyzed. The disease occurred sporadically throughout a large number of different units. Its course was characterized by mildness, with no deaths or complications. Great difficulty was encountered in its early diagnosis because of the complete absence in many cases of historical data and physical abnormalities suggesting pulmonary involvement. The disease was frequently confused with the common respiratory infections and also with commonly occurring tropical diseases, notably dengue and malarial fever. The diagnosis in all cases was finally established by roentgenography.

Four commonly recognized types of roentgen changes were seen: (1) patchy areas of infiltration, of density varying from snowflake to cotton ball appearance; (2) homogeneous areas of infiltration, possibly the result of the confluence of patches, judging from the appearance of the edges of these lesions; (3) infiltration, chiefly in the form of strands, beginning at or near the periphery of the lung fields and converging toward the hilum. These three types of change were invariably limited to a segment of one or more lobes, never involving an entire lobe. Occasionally the only alteration observed was (4) an increase in the prominence of one root shadow without significant parenchymal involvement. Some cases exhibited a combination of two or three of the above types, and in one case all four were observed.

Emphasis is laid upon the value of frequent re-examination as the chief aid in making a differential diagnosis clinically. Although personal contact evidently was important in the transmission of the disease, the suggestion is made that some non-human factor may also have played a part.

Primary Atypical Pneumonia as Seen in the Tropics. Harlan F. Haines and Clark M. Forcey. M. Clin. North America **28:** 1490–1496, November 1944.

This is a report of 40 cases of primary atypical pneumonia observed among American troops on a small island in the South Pacific. The disease was mild and the findings were comparable to those reported by authors elsewhere.

Rib Fractures in Atypical Pneumonia. Rolfe M. Harvey. Am. J. Roentgenol. **52:** 487–493, November 1944.

In a consecutive series of 500 cases of atypical pneumonia occurring in a station hospital, 19 patients had evidence of recent rib fractures. In only one was there a definite history of trauma. A large number of these fractures were missed on the original examination. They were seen later on serial examination of the chest for progress of the pneumonia, after callus had formed. All could have been detected on careful study of the roentgenograms.

The fractures almost invariably occurred in the region of the interdigitations of the muscle fibers of the serratus anterior and the obliquus externus abdominis muscles. All were in the anterior axillary or midaxillary line. Half of the patients affected had multiple fractures It is thought that the mechanism of production is due to opposing forces of the serratus anterior and the obliquus externus abdominis muscles attendant on the strain of coughing. In no case was there any apparent lack of calcium in the bones which could account for the occurrence of the fractures.

Excessive chest pain occurring in cases of atypical pneumonia should direct the search of the roentgenologist toward this complication. It may explain many supposed cases of pleurisy in atypical pneumonia.

The literature on spontaneous rib fracture is reviewed. Reports of cases from the author's series are also given, with reproductions of roentgenograms.

CLARENCE E. WEAVER, M.D.

Early Diagnosis of Pulmonary Tuberculosis. A Review of Cases Revealed in Recruits by Radiological Examination. E. K. MacLeod. New Zealand M. J. **43:** 237–240, October 1944.

Roentgen examination of more than 100,000 army recruits in New Zealand revealed pulmonary tuberculosis, previously unsuspected, in 0.24 per cent, a figure which compares favorably with those obtained elsewhere.

Acute Bronchiolitis in Infants. Edward L. Pratt. M. Clin. North America **28:** 1098–1107, September 1944.

Acute bronchiolitis is an infection of the lower respiratory tract, characterized by the following signs and symptoms: (1) slight malaise and mild irritability progressing more and more rapidly to marked restlessness and great distress, followed by apathy and grave illness; (2) cough and rapid respirations becoming more labored, with inspiratory retractions and prolonged, wheezing expirations; (3) evidence of inflammation of the nose, throat, and ears without significant involvement of the larynx; (4) hyperresonant lung fields in which the breath sounds are diminished; fine dry râles and varying numbers of musical râles widely distributed, although sometimes partially obscured by coarser moist and musical râles.

Chest roentgenograms reveal certain characteristic changes, the most uniform alteration being emphysema involving all portions of the lungs. Bulging of the emphysematous tissue into the interspaces is a prominent feature. Bronchovascular markings are increased, and there is peribronchial infiltration of varying degree. Small patches of pneumonic consolidation or atelectasis may be seen close to the hila and toward the bases. Close inspection of the films reveals irregularity of aeration, due to different degrees of bronchial and bronchiolar plugging, with multiple small areas of emphysema surrounded by normal or partially atelectatic lung tissue. Fluoroscopy is apt to be deceptive, since the lung fields appear unusually

bright and no large areas of increased density are seen. The diaphragm is depressed and moves very little, and the thoracic cage appears to be fixed in the position of extreme inspiration.

The treatment of acute bronchiolitis is directed toward the infection, the respiratory distress, the oxygen lack, and the circulatory collapse. The methods used in combating these disturbances are outlined.

Rôles of Medicine and Surgery in the Management of Bronchiectasis. John Alexander. Ann. Int. Med. **21:** 565–579, October 1944.

The primary cause of bronchiectasis is obstruction of varying degree in the larger bronchi, due to a foreign body, bronchial carcinoma or adenoma, tuberculous granulation tissue or fibrous stricture in the bronchial wall, pyogenic granulation tissue, or extrabronchial pressure by enlarged lymph nodes or other tumors. Important secondary causes are infection of the bronchial walls beyond the site of obstruction, varying degrees of atelectasis, and sometimes parenchymal fibrosis. Bronchial pneumonia is widely recognized as the most frequent initial lesion leading to bronchiectasis.

Many theories have been advanced to explain the mechanism of the development of bronchiectasis. Probably the most satisfactory is the following. Poor pulmonary ventilation results in the stagnation of viscid secretions in the small bronchi; patchy or lobar atelectasis then occurs; the highly negative intrathoracic pressure and, particularly, the pull of inspiration are not absorbed by the inelastic atelectatic part of the lung and so are transmitted to the bronchi, which dilate. If the bronchial walls become infected as a result of the stagnation of secretions (from inadequate ventilation and swelling of the mucosa), the walls become weakened and are likely to remain dilated even after the atelectasis has disappeared.

The diagnosis of bronchiectasis is suggested by the history, symptoms, physical signs and the roentgenographic and bronchoscopic findings. Almost without exception, however, an absolute diagnosis depends upon iodized oil bronchograms. Plain roentgen films show a diversity of shadows frequently confused with tuberculosis, congestive heart failure, atelectasis, bronchiogenic carcinoma, etc. Prior to instillation of iodized oil, lateral, postero-anterior, and stereoscopic films are taken to ascertain in advance as much as possible about whatever abnormal shadows are present.

Iodized oil should not be introduced into the lung within three weeks following the disappearance of an attack of acute pneumonitis or any febrile episode which presumably had its origin in the pulmonary lesions. The breaking of this rule may result in a serious (occasionally fatal) attack of acute pneumonitis.

The persistence of a filling defect in any bronchus proximal to the fourth order in two or more series of bronchograms is of the greatest clinical significance, since such a filling defect indicates not only that there is a probably harmful bronchial obstruction, but also that bronchiectasis presumably exists in the pulmonary segment beyond the obstruction.

A mere list of the complications indicates the potential gravity of bronchiectasis: repeated attacks of acute suppurative pneumonitis; pulmonary abscess or gangrene; septicemia; pleural empyema; spontaneous pneumothorax; brain abscess or meningitis; repeated severe hemoptyses; pulmonary fibrosis, emphysema, cor pulmonale, myocardial degeneration, cardiac decompensation; nephritis and amyloid disease; suppurative pericarditis; arthritis, and carcinoma from metaplasia of chronically inflamed bronchial mucosa.

The aim of treatment is to reduce, as far as possible, the ill effects of the permanent lesions by non-surgical means, or to remove the lesions completely by lobectomy. The latter is overwhelmingly the treatment of choice for those patients (1) whose age, cardiorespiratory functional reserve and general condition are suitable; (2) whose lesions are restricted to one lobe, or to the right lower and middle lobes, or to the left lower and lingular ("left middle") lobes or, in some cases, to all the lobes of one lung (total pneumonectomy) or to one lobe of each lung or to two lobes of one lung and one lobe of the other lung (bilateral lobectomy); (3) who have failed to attain a satisfactorily stable condition of improvement from non-surgical treatment.

Postural drainage is the most valuable of the non-surgical measures. Its aim is to improve bronchial drainage, thereby lessening toxic absorption from retained bronchopulmonary secretions and reducing infection in the bronchi and lung.

Every bronchiectatic patient should have at least one bronchoscopic examination, not only because some otherwise undetectable intrabronchial lesion may be discovered but also because the aspiration of secretions and the chemical shrinkage of the bronchial mucosa often bring about improvement in the symptoms, which in occasional cases is astonishingly great. Bronchoscopy is also of value in preventing the development of bronchiectasis in early cases of pneumonitis or "unresolved pneumonia."

Measures that promote expectoration are beneficial. The usual expectorants and the inhalation of a nebulized spray of a 1:100 dilution of epinephrine solution may prove useful if the secretions are thick and especially viscid.

Treatment of infection in the nasal sinuses, nose, mouth, and pharynx may improve the bronchiectatic symptoms. The author does not recall a single case, however, in which so-called radical sinus surgery carried out in the presence of troublesome bronchiectasis has either completely cured the sinus disease or importantly improved the symptoms of bronchiectasis. STEPHEN N. TAGER, M.D.

Eosinophilia with Pulmonary Disease on Return from the Tropics. J. Apley and G. H. Grant. Lancet **2:** 308–309, Sept. 2, 1944.

A considerable eosinophilia, associated with a cough and a transient pulmonary infiltration, was encountered in an Englishman returning from Bengal. The eosinophilia increased after an attack of acute febrile bronchitis in England. Löffler's syndrome and tropical eosinophilia are compared and it is suggested that the two conditions are not clearly distinguishable.

Löffler's account of the x-ray findings in the chest emphasized the transitory nature of the shadows, and Weingarten (Lancet **1:** 103, 1943) has stated that in tropical eosinophilia "the mottling rarely lasts more than four weeks." This is, however, not invariably true, since Emerson (U. S. Nav. M. Bull. **42:** 118, 1944) recorded a case in which the shadows had actually increased after three months before beginning to clear following arsenical treatment. "Thus," say the authors, "from the mildest case of Löffler's syndrome to

the most severe cases of tropical eosinophilia, there is a gradation in the duration of the shadow."

Spontaneous Pneumothorax and Bronchial Asthma. Hugo T. Engelhardt and Vincent J. Derbes. Ann. Int. Med. **21:** 711–718, October 1944.

The physical signs of pneumothorax associated with asthma do not differ from those of other etiology. Pain, cough, dyspnea, and shock are found. Fremitus, and breath and voice sounds are suppressed. Hyperresonance and displacement of the heart are often demonstrable. The roentgen examination is the *sine qua non* of diagnosis and without its aid many minimal cases would be overlooked. The main point in the differential diagnosis is the exclusion of the tubercle bacillus as the etiologic agent.

The authors report a case in a 48-year-old man complaining of severe dyspnea of three weeks' duration. He gave a history of recurrent attacks of asthma following pneumonia a year and a half before admission. A roentgenogram of the chest showed 50 per cent collapse of the right lung and mottling in the first interspace on the left. The patient was thought to have a right pneumothorax and bronchial asthma. Thoracentesis was done, and 200 c.c. of air were withdrawn from the right hemithorax. On the third hospital day a blowing sound was heard over the right side of the chest, indicative of a possible bronchopleural fistula; 1,300 c.c. of air were withdrawn from the chest on this day. Death occurred two days later.

Autopsy showed no enlargement of the heart. The right lung weighed 550 gm., and the left 390 gm. The former was small and somewhat wrinkled on its surface, which was marked by fibrous adhesions and occasional emphysematous blebs. The pleura was thickened by dense scar and fibrous tissue. In the majority of the sections the alveoli were partially collapsed. All the bronchi were dilated, the fibrous tissue around them being hypertrophied and heavily infiltrated with lymphocytes.

The authors point out that if the spontaneous pneumothorax accompanying asthma were due to an erosion process, it would be followed by pleural infection and pyopneumothorax, but this is not the case. They account for the collapse by the intermediation of a valve vesicle (congenital, emphysematous, or cicatricial). With each respiratory cycle the positive pressure increases in the vesicle because the nature of the lesion allows air to enter more easily than to leave. In this manner a vicious cycle is initiated, so that the pleural covering of the vesicle becomes progressively thinner and, because of diminished blood supply, devitalized. Then, without any appreciable strain, the vesicle tears and a greater or lesser degree of pneumothorax results.

The danger of rupture may be considered greater on deep inspiration than on coughing, since atmospheric pressure is present within the alveoli and a negative pressure without. During coughing, the tendency is toward the closer approximation of the chest wall to the lung, resulting in a decrease in negativity in the intrapleural space and a lessening of the positive pressure in the alveoli. Both these factors act to preserve the integrity of the vesicle. Coughing, however, could tear the lung in marginal zones where the pressure is unequal.

Whereas spontaneous pneumothorax can happen at any age, it usually occurs in early adult life, when negative intrapleural pressure is greatest. The elastic recoil of the lung is greater in youth, the action of the diaphragm is more efficient, and the degree of emphysema is less.

The prognosis in pneumothorax complicating asthma is good, the vast majority of cases going on to recovery with a minimum of therapy or none, provided the patient is not in an acute asthmatic attack.

The removal of air from the pleural space is strongly contraindicated for three reasons: (1) the equality of pressure within and without the alveolus facilitates healing of the torn vesicle; (2) removal of air and the production of a negative intrapleural pressure favor the formation of a bronchopleural fistula, from which a chronic pneumothorax or a tension pneumothorax may result; (3) the existence of a fistula favors the contamination of the pleural space. Tension pneumothorax appears to be the one indication for thoracentesis. Here action is imperative to relieve respiratory distress. After the site of rupture has healed, the use of air-oxygen mixtures where the concentration of oxygen approaches 100 per cent may be of real value.

STEPHEN N. TAGER, M.D.

Pulmonary Cysts. David G. Pugh. Am. J. M. Sc. **208:** 673–681, November 1944.

This paper, appearing under the heading "Progress of Medical Science," is in the nature of a review.

Since the etiologic factors are varied, and perhaps not completely understood, the author believes that pulmonary cysts are probably best classified from a roentgenologic point of view; that is, on the basis of size, shape, number, and distribution. He quotes Sellors' classification (Tubercle **20:** 49, 114, 1938).

Some pulmonary cysts, particularly the "balloon" or "distention" type, which occur in newborn infants, are probably congenital in origin. In the light of studies which indicate that the development of the permanent pulmonary parenchyma of the adult occurs after birth, taking from three to fourteen years for its completion, it is probable that the origin of many pulmonary cysts should be considered "developmental" rather than "congenital." Disturbance in the development of the lung, notably infection in early life, may result in persistence of the primitive infantile type of lung. The bronchi in such a lung may become stretched and distended, and bronchiectatic and cystic structures may occur, depending on whether the bronchi remain patent or become shut off at the proximal end.

It has been emphasized recently that pulmonary cysts are frequently acquired, as the sequelae of bronchitis or bronchopneumonia. A pneumatocele may start as acute lobular emphysema. A check-valve obstructing the bronchial lumen may be due either to non-resolution of the initial inflammation or to a subsequent distortion of the dilated air spaces. In infants with pneumonia there have been reported lesions which resemble congenital cysts, but which are really due to regional obstructive pulmonary emphysema. These usually disappear spontaneously.

Cysts may produce symptoms through the following mechanisms: (1) There may be respiratory embarrassment due to loss of lung tissue owing to the expansion of the cyst, compression of the remaining lung, and mediastinal displacement. (2) Infected cysts may cause symptoms of pulmonary suppuration. (3) There may be enlargement of the right side of the heart and cardiac failure.

Pulmonary cysts are to be distinguished from emphysematous bullae and tension pneumothorax. Infected cysts must be differentiated from lung abscess, tuberculous cavitation, empyema, and cavernous bronchiogenic carcinoma.

Bronchography is not considered to be of much assistance in cases of cystic lung, although it has been used in the attempt at differentiation from empyema. It may also be used to determine the extent and site of cystic bronchiectasis. BENJAMIN COPLEMAN, M.D.

Congenital Absence of the Lung (Agenesis) and Other Anomalies of the Tracheobronchial Tree. Charles F. Ferguson and Edward B. D. Neuhauser. Am. J. Roentgenol. **52:** 459–471, November 1944.

Agenesis of the lung has been encountered so rarely that only about 50 examples have been recorded in the medical literature. The authors have seen 5 cases of this developmental anomaly during the past six years. All 5 were diagnosed during life by bronchoscopic examination followed by lipiodol roentgenograms of the tracheobronchial tree. Four patients are still living.

Males are more commonly affected, though 3 of the authors' patients were females. The left lung is more frequently absent than the right. As to cause, the theory of a developmental error of endogenous origin seems most logical. A great number of cases show coincidental anomalies, such as a narrowed trachea, extra cartilaginous rings, supernumerary bronchi of the normal lung, absence of the pleura on the affected side, tracheo-esophageal fistula, esophageal stenosis, and synostosis of various ribs. In addition, more distant congenital abnormalities have been recorded. Each of the authors' patients had some other developmental anomaly.

Anatomically three types of agenesis are recognized, depending on the age at which the developmental defect occurred in the embryo: (1) true aplasia—cases in which there is no trace of a lung, bronchus, or vascular supply to the affected side; (2) cases in which there is a tiny out-pocketing of the trachea; that is, a primordial bronchial bud, but no lung tissue; (3) extreme hypoplasia, in which the bronchus is fully developed, but reduced in size, ending in a fleshy structure without lobes, which lies in the mediastinum. Most cases fall in the first category—true aplasia.

Symptoms are variable or may be altogether lacking. In practically every case the potentially vacant space in the chest is filled with displaced heart, thymus, and other mediastinal contents. The roentgenograms generally show a dense homogeneous shadow on the affected side, with displacement of the heart and mediastinum to that side and with elevation of the diaphragm and narrowing of the intercostal spaces. Bronchoscopy is the only rational and final method for accurate clinical diagnosis. Lipiodol injection at the time of bronchoscopy should solve the problem.

Prognosis should always be guarded, although the condition is compatible with longevity. In cases of persistent emphysema or atelectasis, or cases of supposed unresolved pneumonia or recurrent pneumonia in the same lobe, congenital anomalies of the tracheobronchial tree must be considered.

Case histories of five patients with agenesis of the lung are presented, accompanied by roentgenograms and bronchograms. Bronchograms of five cases of tracheobronchial tree anomalies are also presented.

CLARENCE E. WEAVER, M.D.

Abscesses of the Lung in a Premature Baby. William Leach and Mark Holland. Am. J. Dis. Child. **68:** 324–326, November 1944.

The authors' patient was a six weeks premature infant seen at the age of two and a half months. Delivery had been normal, and the child appeared to be thriving when an intermittent fever developed, with an unproductive cough. Examination showed signs of pneumonia in the right lung and sulfathiazole therapy was instituted. Symptoms and signs increased in severity during the next forty-eight hours with but little rise in temperature. Thoracentesis produced 20 c.c. of thick pus which contained staphylococci. A second aspiration, six days later, following a severe unproductive spasm of coughing, yielded 30 c.c. of similar material. A chest roentgenogram at this time showed little evidence of pleural fluid and revealed three large circular areas of decreased density with rather thick walls, apparently cavities, occupying most of the right lung. A second roentgenogram, three weeks later, showed the cavities to be slightly smaller, with no pleural reaction. Clearing thereafter was progressive, so that only accentuation of the peribronchial markings in the middle part of the right lung remained after eight months.

The authors assume these lesions to have been pulmonary abscesses, although no fluid levels in the cavities were ever described nor can they be detected in the excellent roentgen reproductions. In addition, there was no history of preceding upper respiratory disease, foreign body aspiration, or operative procedure.

LESTER M. J. FREEDMAN, M.D.

Pulmonary Disease Associated with Mega-Esophagus. H. Stephen Weens. Am. J. Roentgenol. **52:** 472–480, November 1944.

A review of the literature reveals little attention to the occurrence of pulmonary lesions accompanying mega-esophagus. During the past four years the author has observed 15 cases of this latter disorder and in 5 of these cases pulmonary disease was demonstrated roentgenologically. One patient had an abscess in the upper right lobe. Another showed the presence of acute and chronic pulmonary disease consisting of aspiration pneumonitis and interstitial fibrosis. In a third case there was diffuse interstitial pulmonary fibrosis. A fourth patient had aspiration pneumonitis in both lung bases. In the fifth patient there was an associated bronchiectasis.

It should be emphasized that the digestive disturbances of mega-esophagus, especially in the presence of respiratory symptoms, may appear so slight to the patient that he will frequently conceal their presence. Among the roentgen evidences of mega-esophagus is widening of the mediastinal shadow toward the right side, extending from the base of the neck to the diaphragm. A fluid level in the esophagus is a helpful sign. Another observation of great significance is a double air column overlying the upper dorsal spine in the postero-anterior view. The central air column represents the trachea, which is seen through the air column of the upper dilated esophagus.

In all patients with mega-esophagus, the presence of pulmonary disease should be suspected and searched for. Similarly, in patients with pulmonary disease of unknown etiology, the presence of mega-esophagus should be taken into consideration. It is believed that the pulmonary lesions are the result of aspiration of esophageal contents.

Five case reports with reproductions of roentgenograms are given. CLARENCE E. WEAVER, M.D.

Pulmonary Suppuration Secondary to Cardiospasm. I. Bird-Acosta. Am. J. Roentgenol. **52:** 481–486, November 1944.

There are numerous causes of esophageal retention. Of these, cardiospasm, though a fairly common clinical entity, is rarely considered when an explanation is sought for a chronic pneumonitis of unknown origin. The pulmonary suppuration is the result of esophageal overflow and aspiration of esophageal contents. Three cases of this nature are described in detail, and reproductions of roentgenograms are included.

CLARENCE E. WEAVER, M.D.

Scrub Typhus. Results of a Study of the Cases of Two Hundred Patients Admitted to and Treated at a Station Hospital between Feb. 9, 1943, and Feb. 4, 1944. Bernard L. Lipman, Adrian V. Casey, Robin A. Byron, and Edwin C. Evans. War Med. **6:** 304–315 November 1944.

This comprehensive paper on scrub typhus, based on a series of 200 cases treated in the Southwest Pacific area, includes a section on pulmonary complications which should be of interest to radiologists. In the majority of the patients the earliest observed pulmonary abnormality was inspiratory and expiratory sonorous râles, occasionally associated with a mild degree of cyanosis. In 20 per cent of the series physical signs of bronchitis developed during the course of the disease. These included harsh breath sounds, a few scattered râles, and cough, productive of some mucopurulent sputum, which was occasionally blood-tinged. Roentgen examination in such cases either revealed no abnormality or showed increased bronchovascular and hilar markings. The bronchitis may overshadow an underlying rickettsial pneumonitis, such as exists in Q fever. With the subsidence of the fever and concomitant clinical improvement, the signs of the bronchitis or pneumonitis disappear. Nine per cent of all the patients contracted bronchopneumonia, and this diagnosis was confirmed by roentgen examination. Four per cent of the total number acquired lobar pneumonia with typical physical signs. Five per cent of the patients had pleural effusion, bilateral in 2. Three patients had bronchial asthma during the course of the disease; none of these had previously experienced asthmatic attacks. Large pulmonary emboli proved fatal in 2 cases. Lobar atelectasis occurred once, in a patient with a chest wound.

Mediastinal Emphysema Resulting from Exposure to a Pulmonary Irritant. Raymond W. Monto and Paul S. Woodall. War Med. **6:** 251–252, October 1944.

A case of mediastinal emphysema in a young man, resulting from exposure to chlorine gas, is reported. The diagnosis of interstitial emphysema was established by the characteristic crunching sounds synchronous with the heart beat heard in the precordial area. It was confirmed by the roentgen finding of air at the base of the neck in the deep fascial planes.

Value of Roentgenologic Examination of the Heart. M. L. Sussman and A. Grishman. Am. Heart J. **28:** 647–660, November 1944.

The authors present an angiocardiographic study of the heart contours in the normal subject and in those diseases in which there occurs predominant enlargement of a single chamber. The observations were confirmed in most instances by postmortem correlation.

Normally, in the postero-anterior position the right heart border is formed by the right auricle. At its junction with the supracardiac segment there is ordinarily some portion of the ascending aorta. The aortic valve is situated a variable distance within the cardiac silhouette. The lower left contour is formed by the left ventricle, and above this is the pulmonary artery. Between the two there is usually a small segment which is not demonstrable in the usual angiocardiogram but is thought to be the left auricular appendage. The pulmonary valve is also hidden in the cardiac silhouette. The pulmonary conus does not form part of the cardiac contour. In a few cases the descending branch of the left pulmonary artery may be projected so that its shadow merges with that of the pulmonary artery and actually forms the contour of the middle left cardiac segment. As the subject is rotated into the right anterior oblique position, the pulmonary artery forms the entire middle left arc. In the right lateral projection the pulmonary conus also forms part of the contour below the pulmonary artery. In the left anterior oblique position the right ventricle may constitute part of the lower anterior contour in some cases, but most often it is obscured by the right auricle. The lower left border in this position is formed by the left ventricle. The boundaries of the right ventricle cannot be identified in this view. The interventricular groove does not correspond to the position of the interventricular septum as seen angiocardiographically.

Right ventricular enlargement, which is characteristic of cor pulmonale, is indicated by prominence of the pulmonary artery segment even though radiologically the heart may not appear enlarged. In the absence of pulmonary artery dilatation, the only evidence of moderate right ventricular dilatation in emphysema is enlargement of the heart to the left, but this observation is useless unless clinical data exclude *left* ventricular dilatation and a pulmonary disease is present in which cor pulmonale might be expected.

The outstanding example of left auricular dilatation is seen in mitral stenosis. Roentgenologically a straightening or convexity of the middle left cardiac contour is observed in the postero-anterior and right oblique positions. The chamber may be demonstrable as a dense area within the cardiac shadow. Sometimes it projects to the right and overlaps the right auricular contour. In the right oblique and right lateral positions there is encroachment upon the retrocardiac space. The esophagus is displaced posteriorly and to the right and is compressed. Angiocardiograms show elongation, elevation, and anterior bowing of the pulmonary artery, but it is not ordinarily dilated to any significant degree. The right ventricle is also bowed anteriorly. Except when the left auricle is seen directly, the most accurate criterion of its size is the position of the esophagus.

Left ventricular enlargement may take the form of concentric hypertrophy with little or no dilatation (usually associated with hypertension) or eccentric hypertrophy with dilatation. In concentric hypertrophy the contour of the left ventricle is the basis of roentgen diagnosis. The outline becomes more rounded and with increasing hypertrophy there is also elongation of the ventricle. Concentric hypertrophy with dilatation is manifested first by an increase in the size of the left ventricle, particularly in its long diameter, accom-

panied usually by enlargement to the left and posteriorly. The authors are not in agreement with those who believe that, when the long diameter of the heart exceeds the transverse diameter by more than 10 per cent, enlargement of the left ventricle may be assumed, for the long diameter is not a true indication of the length of the ventricle. Therefore, until the increased volume is detectable by measurement of the whole heart, it is necessary to rely upon visual impression to ascertain whether the left ventricular contour is abnormal.

In their conclusion, the authors point out that the roentgen examination is only a part of the study of the heart. Only as the findings are considered critically in association with other clinical data do they become of real value. Alone they may be insignificant or even misleading. HENRY K. TAYLOR, M.D.

On the Circulation Through the Heart, the Big Vessels and the Pulmonary Circulation, Simultaneously Recorded by Cinematography and Electrocardiography. Nils Westermark. Acta radiol. **23:** 473–510, Oct. 31, 1942. (In English.)

This article, which assumes the importance and proportions of a monograph on the subject of cinematographic and electrocardiographic demonstration of circulatory phenomena, does not lend itself to adequate abstracting within the limited space of RADIOLOGY and should be read in the (English) original by anyone interested in this outstanding research work.

The author himself summarizes his experiments and findings as follows:

"By injecting thorotrast as the contrast medium the circulation through the heart and the big vessels has been recorded by roentgencinematography at a rate of 32 pictures per second. Electrocardiography has been simultaneously carried out. This permits the film pictures to be compared with the electrocardiograms with an accuracy of 0.03 sec.

"The circulation time through the lesser circulation has varied between 1.4–2.5 sec. with an average of 1.7 sec.

"The maximal circulatory rate in the pulmonary artery during systole is found to be 150–200 cm./sec. and in the aorta 350–650 cm./sec. The mean rate of flow during systole and diastole is 25–30 cm./sec. and 35/65 cm./sec., respectively.

"The circulation through the heart shows that the atrio-ventricular valves open at P and close immediately before Q. It is only during this period that the ventricle seems to fill up with blood. During this period the auricle empties itself only in part and apparently forms a blood reservoir holding large quantities of blood-rests. The auricle is getting filled up all the time, with a more rapid filling immediately after the T wave at the beginning of the diastole.

"The systolic contraction of the ventricle begins in conjunction with the QRS complex with a downward movement of the atrio-ventricular junction. In so doing the junction seems to bulge into the ventricle like a cone. The downward movement of the atrio-ventricular junction is probably caused by contraction of the interventricular septum. Then the ventricular wall begins to contract at the apex at the same time as the atrio-ventricular junction is seen to make a regressive movement between the S and T waves. During this period the space between the atrio-ventricular junction and the inner contour of the ventricular apex seems to be unaltered. The ventricular wall then continues its contraction successively up to the conus arteriosus.

"This progressive course of the contraction of the ventricle accords well with Lewis' investigations into the excitation of the ventricular wall, its distribution and duration.

"The semilunar valves do not seem to open until the beginning of T when the contraction wave through the ventricular wall reaches the conus and when the ventricular pressure has attained its maximum. The closure of the semilunar valves takes place at the end of T. The ventricle has then almost completely emptied itself and afterwards seems to stand under prolonged contraction holding a slight amount of blood-rests. At the P wave the ventricle is seen to relax and the atrio-ventricular valves to open at the same time as the next phase sets in.

"The different phases of contraction of the ventricle and auricle also seem to be reflected in the pressure curves from auricle, ventricle, and aorta."

ERNST A. SCHMIDT, M.D.

Rupture of Mitral Chordae Tendineae. Clinical and Pathologic Observations on Seven Cases in Which There Was No Bacterial Endocarditis. Orville T. Bailey and John B. Hickam. Am. Heart J. **28:** 578–600, November 1944.

The histories and pathologic observations in 7 cases of rupture of the mitral chordae tendineae unassociated with bacterial endocarditis are reviewed. All showed fibrosis and chronic injury of the mitral valve. In two, the lesions were those of rheumatic heart disease; in the remainder, the changes suggested quiescent rheumatic disease, but were not pathognomonic. The roentgen findings are of particular interest. In 2 of the 4 cases examined a moderate dilatation of the left atrium was observed. In neither of these cases was there a significant mitral stenosis at autopsy. In one case the left atrium exhibited a systolic pulsation. This is a sign of very brisk mitral regurgitation. Dr. M. C. Sosman, in a personal communication to the author, stated that he has noted this finding in two other patients who are still living and feels that it is strongly suggestive of rupture of the mitral chordae tendineae. If further study confirms this, the observation will be of great assistance in the diagnosis of the condition.

THE DIGESTIVE SYSTEM

Diagnostic Delay in Gastric Carcinoma. Gilson Colby Engel. Pennsylvania M. J. **48:** 126–129, November 1944.

More deaths are caused by cancer of the stomach than by cancer of any other organ of the body, deaths per 100,000 population being 29.6 as compared with 14.9 for cancer of the female genital organs and 10.4 for mammary cancer. In only 17 per cent of cases seen by the author is there any hope of cure, and this figure does not differ greatly from those of other clinics. "The finger of guilt," he says, "must point to delay"—delay in appearance of symptoms, delay on the part of the patient in seeking medical advice, delay by the physician in making a diagnosis and in seeking surgical consultation. To these causes of high mortality must be added inadequacy of surgical procedure.

The three chief diagnostic tests for early carcinoma of the stomach are gastric analysis, roentgenography, and gastroscopy. The author states that with nega-

tive x-ray findings and a positive history there is still a 25 per cent chance of an ulcer or carcinoma being present and that the chance of error in differentiating between a benign and a malignant lesion is about 50 per cent. Added to this possible error is the further fact that in about 80 per cent of gastric carcinomas the symptoms disappear on an ulcer regime. The accuracy of gastroscopic examination is given as about 75 per cent, and of gastroscopic and roentgen examination combined as 85 per cent.

The indications for operation are listed as follows:

1. Gastric lesion with low acidity.
2. Gastric lesion—middle age—loss of appetite—tired.
3. Gastric lesion—greater curvature of posterior wall.
4. Large prepyloric lesion regardless of acidity.
5. Fundal lesion or high lesser curvature lesion.
6. Obstructive gastric lesion.
7. Penetrating gastric lesion.
8. Gastric lesion with hemorrhage in patient over 45 years old.
9. Medically treated gastric lesion—four to six weeks' treatment and still a positive x-ray.

JOSEPH T. DANZER, M.D.

Diverticulitis of the Distal Colon. Harold G. Reineke. Ohio State M. J. **40:** 939–941, October 1944.

Diverticula are the most common of all lesions of the large bowel. While usually of no immediate clinical importance, they may give rise to several secondary processes; of these, diverticulitis is the most important. Diverticula may be demonstrated either by the barium meal or by barium enema. If the clinical evidence points to the colon as the seat of the trouble, the enema study should be performed first. This materially lessens the danger of making a partial obstruction a complete one. The enema should be given under fluoroscopic guidance so that the contours and movements of the bowel can be studied from all angles. Spot films taken on the fluoroscopic table as the column of barium progresses sometimes furnish information not revealed by those of the completely filled colon. Post-evacuation films are of great value and will often show diverticula which were not seen when the colon was full. Failure of the diverticulum to fill immediately is attributed to swelling of its mouth or to the presence of bowel contents which prevent entrance of the barium.

A differential diagnosis between obstruction due to diverticulitis and that produced by carcinoma cannot be made roentgenologically, unless some of the barium passes through the constricted area. Carcinoma destroys the mucosa and produces a margin on which no mucosal pattern can be seen, while in diverticulitis the mucosal folds persist and are usually exaggerated. Serial roentgenograms are of great assistance. The constriction due to tumor remains unchanged in size and shape while the inflammatory constriction may vary from time to time in its more intimate detail. A cancerous constriction is usually relatively short and the adjacent walls, as a rule, fill out widely and flexibly; in diverticulitis the constriction is usually relatively longer and the adjacent gut is likely to be irritable. Diverticulitis and carcinoma rarely occur in the same person.

The patient with complete obstruction must have a cecostomy. Following this, he should again be examined roentgenologically in an attempt to arrive at the correct diagnosis. In some cases of diverticulitis, the inflammation has been found to subside and further surgery has been unnecessary.

Meckel's Diverticulum: Preoperative Roentgen Diagnosis. Glenn D. Carlson. Mil. Surgeon **95:** 272–274, October 1944.

A case of Meckel's diverticulum, diagnosed preoperatively by roentgen studies, is presented. The author advocates the utilization of frequent roentgenograms and fluoroscopy during the four to six hours following the barium meal as affording greater opportunity for the demonstration of diverticula, abnormal mucosal patterns, and other intestinal variations. He believes that the number of small bowel lesions demonstrated is in proportion to the amount of time and study devoted to examination.

Diagnosis of Liver Abscess by Means of Thorotrast Hepatosplenography. Wallace M. Yater. J. A. M. A. **125:** 775–778, July 15, 1944.

A brief discussion is presented of liver abscess, both amebic and pyogenic, with reference to the diagnostic efficacy of hepatosplenography following thorotrast injection. The adult dose of thorotrast is 75 c.c. and the x-ray exposures are made several hours after injection. Details of the technic are given. Reference is made to a previous study of 286 patients, on whom this procedure was used without harmful effects (Yater and Coe: Ann. Int. Med. **18:** 350, 1943. Abst. in Radiology **41:** 410, 1943).

The abscess is demonstrable as an area of lesser density than the normal liver tissue. Metastatic carcinoma also appears as an area of decreased density but is frequently surrounded by a halo of condensed liver tissue, which serves as a differentiating feature. Solitary tumors are unusual but present roentgenographic features similar to those of metastatic growths. The same is true of echinococcic and other rare cysts.

Five cases of probable amebic liver abscess and 2 of pyogenic liver abscess are presented. Unfortunately the reproductions of the roentgenograms are so poor that little benefit can be obtained from their study.

The author believes that increasing alertness to the possibility of amebic abscess will be necessary in the future because of the likelihood of its occurrence in service men returning from the tropics.

ROBERT S. MACINTYRE, M.D.
(University of Michigan)

Pancreatic Lithiasis with Associated Intestinal Hemorrhage. Report of a Case. Herbert Fanger. New England J. Med. **231:** 678–680, Nov. 16, 1944.

A 63-year-old man had diffuse abdominal pain of one year's duration, with tarry and blood-streaked stools and a loss of 20 pounds in weight. The pain was not referred to the back nor did it show radiation. Blood studies and x-ray examination of the gastro-intestinal tract gave no information. At autopsy, an ulceration 4 mm. in diameter was found near the ampulla of Vater, filled with fresh clot, beneath which was a stone 3 mm. in diameter. Numerous smaller stones were found throughout the pancreatic ducts.

No adequate explanation for the formation of pancreatic stones has been offered and their etiology is unknown. Theoretically, pancreatic lithiasis should be seen on a scout film of the abdomen, but the small

size and low calcium content of the stones probably explain the infrequency of this finding.

JOHN B. MCANENY, M.D.

THE SUPRARENALS

Two Cases of Sympathicoblastoma of the Suprarenal Gland with Metastases to the Cranium and the Tubular Bones. Thomas Rosendal. Acta radiol. **23:** 462–472, Oct. 31, 1942. (In English.)

Two cases of sympathicoblastoma, apparently originating in the suprarenal glands, with extensive osseous metastases are reported.

In the first case, in an 18-month-old boy, metastatic tumors were observed above the left orbit in the frontal bone, in the left mandible, and in the diaphysis of the left radius, as well as in the diaphyses of both femora, tibiae, and humeri. X-ray examination of the abdomen showed a large tumor in the left kidney region with evidence of some small irregular calcifications. The osseous changes were first interpreted as Ewing's tumor or, possibly, osteomyelitis, syphilis, or Schüller-Christian disease. Radiotherapy resulted in temporary improvement only. The microscopic diagnosis following necropsy was sympathicoblastoma of the suprarenal gland with metastases.

In the second case, in a one-year-old boy, fixed tumors in both temporal regions with bilateral exophthalmos were observed, and a large tumor in the right flank could be palpated. Roentgenograms of the cranium showed spicule formation at the bone surface in the temporal region and numerous small bone rarefactions in the right mandible. These bone changes were tentatively diagnosed as hemangioma. A large soft-tissue tumor was demonstrable in the right kidney region, containing numerous minute calcifications. Biopsy of one cranial tumor resulted in the diagnosis of sympathicoblastoma. Following radiotherapy, the bone spicules in the cranium disappeared and there was an improvement of the clinical symptoms, although roentgenographically the destructive bone changes seemed to increase. The patient was still alive at the time of publication (four months after radiotherapy).

Sympathicoblastoma, which seems to be invariably fatal, is rather rare. It has been described as (neurogenic) glioma by Virchow and as retroperitoneal sarcoma of the lymphosarcoma group by Dalton. The roentgenologic differential diagnosis is difficult, as demonstrated and discussed in both cases by the author. In addition to the diseases mentioned above (Ewing's tumor, osteomyelitis, syphilis, Schüller-Christian disease, hemangioma), Wilms' tumor, lymphosarcoma, ovarian tumor, leukemia, chloroma, periostitis, rickets, and other diseases must be considered.

ERNST A. SCHMIDT, M.D.

THE SKELETAL SYSTEM

Roentgenological Diagnosis of Skeletal Diseases of Infants and Children. (Russell D. Carman Lecture of Radiological Society of Minnesota.) Ralph S. Bromer. Minnesota Med. **27:** 895–904, November 1944.

Before discussing the characteristic bone changes in various children's diseases, the author warns against the careless use of the word pathognomonic in this connection. Signs that at one time were considered pathognomonic of a given condition have, with increasing application of roentgen diagnosis to skeletal lesions, been demonstrated in other disease processes as well. The conditions described in the ensuing pages include fetal and infantile rickets, late rickets, renal rickets, scurvy, lead poisoning, leukemia, the chronic hemolytic anemias, sickle-cell anemia, celiac disease, xanthomatosis, Gaucher's disease, and congenital syphilis. Not only does the author present the important roentgen features of each of these diseases, but by frequent reference to the literature he seeks to demonstrate the progress made in their diagnosis in the last two decades.

A reading of the article in the original is strongly recommended, for it does not lend itself to satisfactory abstracting. The zeal and enthusiasm which Bromer has given to the study of roentgen pathology in bone over a period of years are here reflected, as they are in the clarity and comprehensiveness of his many papers on the subject. Particularly has his work been a help in maintaining clear and definitive classifications of the various lesions.

PERCY J. DELANO, M.D.

Leontiasis Ossea Complicated by Marjolin's Ulcer: Observation of a Case for Twelve Years. Ray E. Burger and Edwin P. Lehman. Surgery **16:** 542–556, October 1944.

Virchow applied the term *leontiasis*, which had been used to designate the nodular changes in the soft parts of the face of the leper, to cases presenting hyperostosis of the skull, adding the adjective *ossea*. The name leontiasis ossea is descriptive of the appearance only, not of the actual lesion, the nature of which is still undetermined.

Clinically the disease is characterized by slowly developing bony deformity of the face, usually beginning in early life. If the bony overgrowth impinges on the air passages or the cranial nerves, the syndromes generally known as craniostenosis result. The malady has been compared with acromegaly, but the latter involves the soft tissues as well as the bones. It has also been likened to Paget's disease, but that condition occurs at a more advanced age and is seldom localized to the head. Eden (Brit. J. Surg. **27:** 323, 1939) includes leontiasis ossea among the fibro-osseous tumors of the skull and facial bones under the general designation diffuse osteomas, regarding the lesions as true benign tumors, though he admits the possibility of infection and trauma as irritative factors. The characteristic changes are replacement of the bone marrow by fibrous tissue and, later, an excessive formation of new bone.

The disease usually affects the maxilla, malar bone, ethmoid and nasal bones; less frequently the sphenoid, parietal, and mandibular bones. The involvement may be unilateral or bilateral. Roentgenography reveals thickening and increased density of the bone of intense and uniform character. The surfaces of the affected bone are entirely smooth and sharply defined. The disease does not go beyond the anatomic margins of the bone or of a part of the bone if the latter has developed from more than one bony anlage.

The authors' patient was a man of 28, who had always had a very large lower jaw. This had caused him no discomfort until about six years before admission, when he began to experience pain and swelling of the jaw on the left side and to expectorate blood and pus. Some dead bone was removed at this time and the symptoms were relieved, but a salivary fistula remained. Five months before the present admission there was a

recurrence of the earlier complaints. The lower jaw was large and protruding, and the maxillae were prominent. The floor of the mouth was lengthened forward and many teeth were missing. Several sinuses from the infected left mandible opened through the mucous membrane, and a salivary fistula was present on the right. X-ray examination revealed a large mass of osteoid tissue projecting from the lower jaw at its anterior portion. The maxillae also showed dense new bone formation extending into the antra. No abnormality was seen in the calvarium, shoulder girdle, pelvis, or long bones. Laboratory examination was essentially negative. Two operations were performed on the left jaw for removal of necrotic bone, and several months later a sequestrum was removed.

After an interval of eleven years the patient was again seen. The jaw had meantime grown progressively larger and the tumor had increased in size, extending downward and resting on the chest. It now measured 32 × 22 × 22 cm. and presented large superficial ulcerations. The salivary fistula remained open. Part of the maxilla had sloughed, leaving a mucosa-lined communication between the mouth and the antra, which the patient kept closed with wads of tissue paper. X-rays revealed a tremendous increase in the size of the mandibular tumor, with involvement of the base of the skull and upper cervical vertebrae. Other bones showed no abnormalities except for an old fracture of the left femur.

The tumor was resected with considerable difficulty and the defect covered with skin flaps. The huge, stony hard mass measured 33 × 21 cm. and weighed 6,035 gm. A fistula partially lined with epithelium connected the superior aspect of the specimen with a large irregular area of ulceration. The entire tumor was found to be composed of calcified material resembling cancellous bone with abundant pearly gray fibrous stroma. Many large areas of necrosis were seen. There was no evidence of the formation of bone marrow. The entire mass had the appearance of a benign bone tumor.

Sections of the buccal fistula and the adjacent ulceration revealed epidermoid carcinoma, grade 1. This the authors regard as of the same nature as Marjolin's ulcer occurring in chronic ulceration of the skin and chronic sinuses.

The patient did well for a while but ultimately died of recurrent carcinoma. J. E. WHITELEATHER, M.D.

Pantopaque: Notes on Absorption Following Myelography. George M. Wyatt and Roy G. Spurling. Surgery **16:** 561–566, October 1944.

Lipiodol and the gases formerly used for myelography by the Army Medical Corps have been replaced by pantopaque, its chief advantage being that it is absorbed rather than remaining as a persistent foreign substance in the subarachnoid space. The study reported here was prompted by observations at the Walter Reed General Hospital suggesting that this absorption might not be so rapid in all patients as was previously believed.

Follow-up roentgenograms were obtained for 6 patients in whom the removal of pantopaque had been incomplete. The films included the skull and entire spine and sacrum to exclude the possibility of migration of the contrast material. As judged by the x-ray shadows, there was a definite decrease in the amount of residual pantopaque in all cases. The size and density of the remaining droplets showed that this decrease was due to absorption of the entire compound rather than of iodine only. In several instances minute residual droplets were as opaque to the x-ray as larger droplets seen immediately following incomplete removal. If the decrease in density revealed by x-ray were due to the absorption of iodine from the compound rather than absorption of the total mass, the remaining small collections would have lost their radiopacity.

Absorption was usually most rapid during the first few months following injection. The small remaining droplets were absorbed at a relatively slower rate. The variations in the rate of absorption and in the density of the residual droplets may be due to the nature of the contrast medium, which is a mixture of isomers.

The emulsifying action of body motion on the collection of pantopaque may be responsible for faster absorption in some cases than in others. After a month or two the material becomes fixed in position, which indicates some tissue reaction to the residual pantopaque. None of the patients had any symptoms referable to the residual material.

One patient showed complete absorption of 0.5 c.c. of pantopaque in a period of eleven months.

J. E. WHITELEATHER, M.D.

Variations in Volume and Configuration of the Spinal Canal in Lordosis and Kyphosis; Importance of These Variations for Myelography. Folke Knutsson. Acta radiol. **23:** 431–443, Oct. 31, 1942. (In German.)

Both lordosis and kyphosis produce definite changes in the volume and shape of the spinal canal, as can be demonstrated in anatomical dissections as well as by myelography.

In anatomical specimens of the lumbar vertebrae there is generally a narrowing of the spinal canal at the level of the intervertebral spaces, especially in the region between the 4th and 5th lumbar vertebrae and between the 5th lumbar and 1st sacral vertebrae. This narrowing is caused by increased protrusion of the disk and by more marked bulging of the ligamentum flavum. The latter phenomenon is due partly to forward displacement of the articular portion and partly to increased thickness of the ligament. In kyphosis the lumen of the spinal canal is enlarged. As far as the shape of the spinal canal is concerned, there is visible a more pronounced convex bulging of the ligamentum flavum in lordosis of the lumbar spine and the distance between disk and ligament decreases in the intervertebral foramen.

By means of myelography, it can be demonstrated that, in lumbar lordosis, the narrowing of the spinal canal is accompanied by a corresponding narrowing of the dural sac. In kyphosis this narrowing is diminished. ERNST A. SCHMIDT, M.D.

Hemangioma of the Cervical Vertebra with Fracture and Myelomalacia. Olav Holta. Acta radiol. **23:** 423–430, Oct. 31, 1942. (In English.)

According to Schmorl, Junghanns and others, the pathological study of autopsy material demonstrates the occurrence of hemangioma in the spinal column in about 10 to 12 per cent of all examined cases. Junghanns' series included 409 spines, with 579 hemangiomata. In about two-thirds of these cases, the hematoma was single. The thoracic spine was most often involved (about 60 per cent), followed by the lumbar

spine (about 30 per cent); hemangiomas of the cervical and sacral spine were relatively rare (about 5.5 and 4.5 per cent, respectively).

In the majority of the cases, these tumors are small and centrally located. Clinical symptoms do not appear unless the hemangioma reaches the vertebral surface and affects the adjacent parts, especially the spinal medulla. More or less pronounced transverse lesions of the spinal cord may arise from (1) extension of the hemangioma to the spinal canal, (2) compression by thickening of the vertebral body and arches, and (3) compression fractures of the vertebrae. Roentgenologically, vertebral hemangioma shows marked rarefaction of the spongiosa, resulting in the development of a coarse trabecular structure. In the differential diagnosis, other tumors, hyperparathyroidism, leukemia, and lymphogranulomatosis are to be considered. Symptomatic improvement has been reported following radiation therapy. In cases of definite compression symptoms, laminectomy may bring temporary relief.

The author presents a case of hemangioma in the cervical spine. The patient was a 66-year-old man with the history of a moderate trauma to his head, five weeks prior to hospital admission. The x-ray examination revealed a hemangioma in the 4th cervical vertebra combined with compression fracture and compression myelomalacia. The patient grew progressively worse and died within three months.

The importance of the x-ray examination for determining the diagnosis, extent, and prognosis of the lesions is emphasized. ERNST A. SCHMIDT, M.D.

Aseptic Necrosis in the Epiphyses of Digital Phalanges and Metacarpal Bones (Thiemann's Disease; Dietrich's Disease). Sigurd Franck. Acta radiol. **23:** 449–454, Oct. 31, 1942. (In English.)

Aseptic necroses in the digital phalanges and metacarpal bones were first described by Thiemann in 1909. Since that time, numerous authors have reported cases. Franck describes the case of an 18-year-old male with restricted mobility of the fingers and swelling of the interphalangeal joints. The roentgenograms of the right hand showed flattening of the head of the first metacarpal, a small bone defect in the head of the second metacarpal (combined with sclerosis of the surrounding tissue), smaller bone defects in the head of the first phalanx and in the base of the second phalanx, as well as irregularity of the interphalangeal interspaces in the fourth and fifth fingers, with small exostoses. Similar changes were observed in the left hand. The x-ray changes are interpreted as indicative of a terminated growth disturbance (epiphyseal necrosis) in the epiphyses of the digital phalanges combined with slight arthrosis.

The literature on the subject is reviewed, and, in addition to the roentgenologic and clinical aspects, the etiology and pathology of aseptic necrosis are discussed.

ERNST A. SCHMIDT, M.D.

March Fractures: A New Concept of Their Etiology and a Logical Method of Treatment. Louis W. Breck and Norman L. Higinbotham. Mil. Surgeon **95:** 313–315, October 1944.

The authors believe that the actual mechanism of march fracture is similar to crystallization of steel under prolonged variable stress with its resultant fracture. It is postulated that minute bending of the metatarsal occurs with each step during a march; in response to this prolonged intermittent stress a molecular rearrangement takes place in the calcium phosphate in the bone which renders it brittle and causes it finally to fracture. This theory, although arrived at independently, is not entirely new, as it has been mentioned by various European authors.

During the first six months of 1943, 60 cases of march fracture of the metatarsus were seen by the authors. Excellent results were obtained in 48 cases, poor results in 5 soldiers with previously symptomatic poor feet, and a questionable result in 1 case. Treatment consisted in the use of crutches for four weeks, with complete restriction of weight-bearing.

March Fracture in Industry. James H. Eddy, Jr. New Orleans M. & S. J. **97:** 171–173, October 1944.

Three typical cases of march or fatigue fracture of the metatarsals in women employees of a shell-loading plant are recorded. Concerning the compensation aspects of such injuries the author says: "The problem is extremely difficult as it does not fulfill the requirements of an accident. In this state (Louisiana), however, the compensation act provides for the payment of compensation in all injuries received by an 'employee in performing services arising out of and incidental to his employment.' Under this interpretation of the law it has been advised that these cases be accepted under the compensation act."

GYNECOLOGY AND OBSTETRICS

Growth and Development of the Pelvis of Individual Girls Before, During, and After Puberty. William W. Greulich and Herbert Thoms. Yale J. Biol. & Med. **17:** 91–97, October 1944.

To study the changes in the size and shape of the superior aperture of the female pelvis during puberty and adolescence, 107 girls, ranging in age from five to fifteen years at the inauguration of the study, were examined at approximately annual intervals over a period of four or five years. Ten of the girls were re-examined six years after the original examination. On each occasion the girls were weighed and measured, the degree of development of various secondary sexual characters was recorded, and anteroposterior and lateral x-ray films of the pelvis and a postero-anterior film of the hand and wrist were made.

The pelves of the majority of prepuberal girls (three to four years before menstruation) were found to be long oval in shape, with a pelvic index greater than 95, *i.e.*, they were dolichopellic, according to Turner's classification. At this stage the pelvis was characterized by an acetabular constriction, formed by an inward projection of the pelvic walls into the pelvic canal medial to each acetabulum.

During the years just before puberty, the superior pelvic aperture grew slowly and symmetrically. At puberty, the pelvis began to widen more rapidly than it increased in its anteroposterior diameter, the forepart widened and became more rounded, and the acetabular constriction began to disappear. These changes, which effect a virtual remolding of the superior pelvic aperture and the pelvic canal, required about eighteen months for completion. After the remolding of the pelvis was completed, there was little further increase in size and practically no change in shape in those girls who were followed to early adulthood.

The puberal remolding of the pelvis began after the "bud" stage of breast development had been attained and after some pubic hair had appeared. Axillary hair was not usually present until the pelvic remolding had begun. The pelvic changes were always under way before the occurrence of the menarche and the fusion of the epiphyses of the distal phalanges of the hand.

Their constant position in an orderly sequence of puberal changes that are known to be hormonally determined suggests a similar endocrine basis for the rapid growth and remolding of the pelvis which occur during puberty.

Eight plates are appended. Each consists of a series of films of the pelvis of the same girl, made at intervals over a period of years.

THE GENITO-URINARY SYSTEM

Injuries of the Urinary Tract Complicating Fractures of the Pelvis. T. H. Sweetser. Minnesota Med. **27:** 812–816, October 1944.

Among 103 consecutive cases of proved fracture of the pelvis treated in the Minneapolis General Hospital in the last five years, gross injury to the urinary tract occurred in 12 and there was unexplained hematuria in 30 others. Among the 12 cases of gross injury, were 2 of rupture of the bladder, 3 of rupture of the posterior urethra, and 2 definite renal injuries.

Diagnosis of urinary tract involvement depends mainly on the history and physical findings, supplemented by intravenous urography or catheterization and cystography with an organic iodide solution, such as skiodan, diodrast, or neoiopax. In dealing with recent trauma, intravenous urography may be employed if the blood pressure is high enough to insure good renal output. If results are not satisfactory, a soft rubber catheter may be passed (though too much reliance cannot be placed on the findings) and 2 or 3 ounces of an organic iodide solution introduced through this. The use of air or sodium iodide is not recommended. Cystoscopy is considered too dangerous and would usually be valueless.

Injury of the bladder or deep urethra requires early surgical treatment to avoid disaster, suprapubic cystostomy with drainage of the perivesical tissues being the essential feature. Exploratory opening of the peritoneal cavity should be a preliminary step in the operation. If the patient's condition permits, tears in the bladder should be sutured or the torn urethra brought into line by a catheter passing through the penile urethra or through a perineal urethrotomy.

Seven case summaries are included and roentgenograms are reproduced. PERCY J. DELANO, M.D.

Renal Dystopia Due to Intra-Abdominal Masses, with a Review of the Literature and Report of Five Cases. H. R. Fishback, Jr. Am. J. Roentgenol. **52:** 521–528, November 1944.

Of 34 cases of splenomegaly, hepatomegaly, pancreatic tumors, and miscellaneous intra-abdominal masses observed either roentgenologically or at operation to see if there was displacement of the kidney, 5, or 14 per cent, showed renal dystopia. Two of these cases showed displacement of the left kidney by an enlarged spleen, one by a pancreatic tumor, one by hepatomegaly, and the fifth by splenomegaly and hepatomegaly. Two were demonstrated by retrograde pyelograms, two by flat plates, and one by an intravenous pyelogram.

A survey of the literature seems to indicate that, while displacement of the kidney by intra-abdominal masses is not common, it nevertheless does occur. Gloor (Acta. radiol. **15:** 467, 1934) explains displacement of the kidney by the spleen as due to (1) pressure of the spleen on a floating kidney, thus dislocating the latter downward, or (2) adhesions between the capsules of the kidney and spleen, causing horizontal displacement of the kidney toward the mid-line. It is important to include the possibility of an intra-abdominal mass in the differential diagnosis of renal dystopia.

CLARENCE E. WEAVER, M.D.

Renal Ectopia: Report of 6 Cases. Ormond S. Culp. J. Urol. **52:** 420–429, November 1944.

During urologic study of 747 patients, the author found 6 cases of renal ectopia. Three were of the unilateral variety; 2 were crossed ectopia with fusion, and 1 crossed ectopia without fusion. All conformed to Daseler and Anson's criteria of renal ectopia: abnormal blood supply, fixation, malrotation, and short ureter (J. Urol. **49:** 789, 1943).

Of the 3 patients with simple unilateral ectopia, one had a staphylococcus infection of the kidney. The other two complained of dull pain on the involved side, but there was no evidence of infection.

In the 2 patients having crossed ectopia with fusion, the ectopic organ was on the left side and below the normally placed kidney. One had nocturnal enuresis without evidence of infection. The other patient passed a urinary calculus before the pyelogram was made, but no other calculi were found.

The patient with crossed ectopia unfused had a hypoplastic ectopic kidney, and the normally placed organ was enlarged and had a double pelvis and ureter. This patient complained only of nocturnal enuresis.

The author found that filling the pelvis on retrograde pyelography reproduced the pain in two patients, indicating that symptoms may be present without secondary disease.

In conclusion, it is pointed out that two patients had no symptoms, two had symptoms due to superimposed disease, and two had symptoms which may have been due to the ectopia itself. JOSEPH SELMAN, M.D.

Contribution to the X-Ray Diagnosis of Ectopic Kidney. Gösta Fallenius. Acta radiol. **23:** 455–461, Oct. 31, 1942. (In German.)

In all cases of apparent absence of a kidney or of inconclusive pyelographic findings, the possibility of renal ectopia should be considered. If neither pyelography nor urography leads to a definite diagnosis, the author's method of simultaneous gas filling of bladder and colon may demonstrate the presence of an ectopic pelvic kidney. A series of 8 cases of pelvic kidney observed at Stockholm hospitals is analyzed.

ERNST A. SCHMIDT, M.D.

Long Standing Hydronephrosis with Associated Urological Disease. Case Report. Vincent J. O'Conor. J. Urol. **52:** 408–414, November 1944.

The author reports a case of giant hydronephrosis and hydroureter of fifty years' duration, due to congenital obstruction at the left uretero-vesical junction. In addition, there existed a hypertrophied prostate and

a diverticulum of the bladder which caused symptoms. A calculus 3 cm. in diameter occupied the lower ureter. The patient withstood prostatectomy, diverticulectomy, and ureteronephrectomy and returned to full-time work at the age of sixty-seven.

EDWIN L. LAME, M.D.

Vesico-Ureteral Reflux. George C. Prather. J. Urol. **52:** 437–447, November 1944.

Majority opinion is that vesico-ureteral reflux in the normal person is exceptional if, indeed, it does exist. After summarizing the literature the author reaches the conclusion that, for reflux to occur, it is necessary to have sustained tonus of bladder musculature as it resists distention, and that the anatomical features of the uretero-vesical junction (principally the length and condition of the intravesical ureter) govern the frequency or incidence of vesico-ureteral regurgitation. The oblique course of the intramural ureter probably provides an additional measure of protection. No sphincter exists at the uretero-vesical junction.

Vesico-ureteral reflux is not uncommon when there is distortion of the uretero-vesical valve (intravesical ureter). Distortion may be caused by an inflammatory process, a malignant neoplasm, or mechanical influence from changes in the bladder, trigone, or bladder neck. There is evidence that an incompetent valve permits direct ascending infection and finally a hydroureter. The cause of the reflux should, therefore, be sought for and remedied.

A case is reported in a soldier with a fracture of the pelvis, incomplete dislocation of the left sacro-iliac joint, intraperitoneal rupture of the bladder, and incomplete rupture of the posterior urethra. Suprapubic cystotomy with splinting of the posterior urethra was performed. After removal of the suprapubic tube, cystoscopy revealed a bladder calculus. A urethrogram nine months after the accident demonstrated an irregular stricture in the posterior urethra and a small bladder with reflux up both moderately dilated ureters. A urogram revealed bilateral pyelectasis. A suprapubic cystolithotomy disclosed an "hourglass" bladder with a transverse fibrous septum on the posterior bladder wall which confined the calculus to the distal or trigonal segment of the bladder. The septum was thought to be a residuum of the previous rupture and closure. It had produced distortion of the ureteric regions and was believed to be a likely factor in causing the reflux. The stone was removed and the septum bisected. Approximately one month later a urethrogram revealed no reflux and another urogram showed remarkable improvement in the pyelectasis. A subsequent urogram was essentially normal.

The author believes that the transverse band and inflammatory changes secondary to cystitis and the stone were contributory factors. The excellent result stimulates interest in the mechanism of vesico-ureteral reflux and the correction of responsible conditions.

CHARLES A. PERRYMAN, M.D.

THE BLOOD VESSELS

Value of Venography in Varicose Veins, with Report of Three Cases. Allison E. Imler, Meredith G. Beaver, and William C. Sheehan. Am. J. Roentgenol. **52:** 514–520, November 1944.

Varicose veins are the most common disorder of the venous circulation of the lower extremity. The obliteration of these superficial channels by various procedures is carried out with the supposition that the deep veins are patent and will adequately handle all the venous return. Barrow (Arch. Surg. **45:** 633–646, 1942) has stated that practically all cases of asymptomatic superficial varicosities show normal deep and communicating veins, while in patients with severe symptoms incompetency of the deep and/or communicating veins is usually present. Varicosities associated with deep venous obstruction or marked stasis of the deep circulation are compensatory and will recur following obliteration. This small but important group of cases should be identified by venographic studies and unnecessary or improper operative interference prevented. Even in the presence of almost complete stasis of the deep veins, patency tests may indicate an adequate circulation.

A 35 per cent solution of diodrast is the most commonly used contrast medium. A sensitivity test should be done to avoid serious sequelae. The authors cite three cases in which venograms demonstrated conditions which contraindicated operative interference for superficial varicosities. In one there were dilatation and stasis in the distal portions of the tibial veins. In another there was congenital atresia of the right external iliac vein, with an anomalous long saphenous vein carrying most of the venous return from the right lower extremity across the abdomen to pass through the left external iliac vein. In the third patient the correlation of the history and the roentgen findings resulted in a diagnosis of healed thrombophlebitis of the left superficial femoral vein, producing a complete obstruction of this vein.

CLARENCE E. WEAVER, M.D.

The Roentgenogram in Floating Thrombus. Gösta Fallenius. Acta radiol. **23:** 444–448, Oct. 31, 1942. (In German.)

Phlebography by means of perabrodil, which has become a routine method in varicosities of the lower extremities has in late years been extended to the diagnosis of thrombosis. Due to the high specific gravity of the contrast medium, better roentgenograms are obtained in vertical position of the leg than in horizontal position.

The phlebographic picture of thrombosis varies according to localization and extent of the lesion. Roentgenologically, deficiency or irregularity of contrast filling in a smaller or larger part of the venous circulation suggests the diagnosis, which may be further confirmed by the demonstration of collateral circulation. If this collateral circulation is absent or little developed, the thrombosis is probably recent; the presence of well developed collateral veins points to post-thrombotic changes. Marginal thrombi may be old; floating thrombi must be of recent origin. In the venous pattern the floating thrombus is characterized in the roentgenogram by a filling defect which is seen free but partly surrounded by a thin layer of radiopaque substance, in the lumen of the vein. The diagnosis of floating thrombus is very important in view of the danger of embolus.

ERNST A. SCHMIDT, M.D.

Aneurysm of the Anterior Tibial Artery. With a Note on Arteriography. Martin Fallon. Lancet **2:** 270–272, Aug. 26, 1944.

In open wounds the amount of damage to vascular structures can be estimated and the appropriate treat-

ment carried out at the primary operation. Serious vascular lesions resulting from slight penetrating or perforating wounds of the multiple type, so common in this war, may, on the other hand, conceivably be overlooked. In some cases, the initial vascular injury may be limited to a slight contusion or even a small tear of the vessel, both of which may resolve. In others, the tendency is for the effects of the injury to progress, and the vessel either ruptures spontaneously into the tissues or an aneurysmal sac slowly forms, or both.

A case of traumatic aneurysm, which was unsuspected until some months after the injury, is reported. The patient was wounded by mortar fire on Sept. 5, 1943, a small fragment of metal entering the left leg anteriorly about two inches below the tuberosity of the tibia. This injury seemed to cause little discomfort, but there was swelling of the leg. With bed rest, the swelling disappeared and the patient was discharged to his unit seven days after his injury. He managed his duties fairly satisfactorily, although his leg became stiff and tense after any exercise, and at times he thought it was weaker. There were no skin changes. On Dec. 19, the leg was very swollen. On Jan. 7, 1944, roentgenography showed a small foreign body lying posterior to the interosseous membrane. At this time there was a gross, uniform swelling of the whole left leg below the knee. There were no pitting on pressure, no skin changes, and no enlargement of the superficial veins. The movements of the ankle joint were normal but no tibial pulses could be detected. The limb was elevated in bed and after a week the swelling had subsided except for a more localized area in the upper part of the leg, which was obviously pulsatile. In front, the area was circumscribed and appeared subcutaneous at one point. Behind, it was much less defined and extended over a wide area deep to the calf muscles. A loud systolic bruit synchronous with arterial pulse was heard on auscultation. This disappeared when the femoral artery was compressed in the groin. The posterior tibial pulse was present at the ankle, but the anterior tibial pulse was only just perceptible. Fluoroscopy showed the foreign body lying posterior to the interosseous membrane and immobile. The aneurysmal sac was obviously continuous through the interosseous membrane and from its anatomical position could be derived from either or both tibial arteries.

Arteriography was carried out to determine the exact size, shape, and anatomical location of the sac. Iodoxyl ("Pyelectan" Glaxo) was the only contrast medium available. The femoral artery was exposed by a small transverse incision in the groin and 20 c.c. of iodoxyl was injected into the vessel in ten seconds, the vessel being compressed above. Films were taken at intervals of two seconds from beginning of the injection, six films in all. There was fairly brisk hemorrhage from the puncture site after removal of the needle, but this was easily controlled by digital pressure and ceased entirely after five minutes. It could, however, be a serious complication to a blind puncture of the vessel.

The third arteriogram in the series, taken six seconds from the start of the injection, shows the outline of the popliteal artery and the beginning of the anterior tibial artery with articular branches to the knee. The aneurysmal sac is clearly shown and it is constant for the whole series. It is roughly circular in outline, with a niche on its distal border corresponding to the interosseous membrane, and has a prominence anteriorly which overlaps the shadow of the anterior tibial artery. The anterior tibial artery distal to the aneurysm was much wider than the proximal, which may be attributed to the damage to the periarterial sympathetic nerves at the point of rupture of the vessel. The posterior tibial artery was clearly outlined, though much less dense than the first part of the anterior tibial artery, and obviously displaced posteriorly by the aneurysm. The last arteriogram of the series, taken 12 seconds from the beginning of the injection, showed in addition to the sac the small saphenous vein to be the only vessel well filled. The whole of the calf was covered by a complicated network of venous shadows, both superficial and deep, which obscured the arterial shadows.

Operation was performed a week following arteriography and the patient made an uneventful recovery.

Complications Following Arteriography of Peripheral Vessels. Frederick B. Wagner, Jr. J. A. M. A. **125:** 958–961, Aug. 5, 1944.

The author calls attention to the growing importance of arteriography in the more accurate diagnosis of arterial lesions, especially of the extremities, and the earlier diagnosis of bone tumors. At the same time, he points out that this procedure is not without danger. Local and systemic reactions may occur, with both mechanical and chemical factors playing a part in their etiology. A case report illustrates a local complication and the various other local and systemic reactions are discussed. The local reactions consist of hematoma, extravasations, and severe vasospasm lasting several days, the last being usually incident to the use of organic iodine contrast material. Systemic reactions may occur following the introduction of either thorotrast or organic iodides, consisting usually of erythematous eruptions and the picture of vasomotor collapse, subsiding after a short interval. Severe liver disease, nephritis, and uremia are the main contraindications to the use of contrast media. The author believes these dangers may be minimized by proper selection of cases, a wise choice of contrast material, testing for sensitivity to the medium to be used, painstaking technic, and preparedness for prompt treatment.

GUERDON D. GREENWAY, M.D.
(University of Michigan)

ENDOCRINOLOGY

Endocrinology: A Synopsis of Normal and Pathologic Physiology, Diagnostic Procedures, and Therapy. Edward C. Reifenstein, Jr. M. Clin. North America **28:** 1232–1276, September 1944.

In a comprehensive discussion of endocrinologic physiology, diagnosis, and treatment, the author lists roentgen studies which are of aid in the diagnosis of endocrine disease:

X-Ray Examination of the Skeleton. Bone age is delayed in panhypopituitarism, other cases of pituitary underfunction, hypothyroidism, and hypogonadism; it is increased in precocious puberty.

Wide thoracic vertebrae are seen in acromegaly; crushed, wedged, or "codfish" vertebrae in postmenopausal or senile osteoporosis or the osteoporosis associated with Cushing's syndrome; vertebral "epiphysitis" in long-standing gonadal deficiency; increased density in metastases from carcinoma of the prostate, sometimes simulating Paget's disease.

Roentgenograms of the long bones, jaws, ribs, and pelvis may show cysts and "brown" tumors in hyperparathyroidism; increased density of bones in hypoparathyroidism; metastases from carcinoma of the prostate.

Terminal tufting of the phalanges is found in acromegaly.

Skull plates show sella turcica changes in the presence of pituitary tumors; calcification in suprasellar cysts; osteoporosis in Cushing's syndrome; decalcification in hyperparathyroidism; calcification of the choroid plexus and density of bone in hypoparathyroidism.

Dental films may reveal an absence of the lamina dura in hyperparathyroidism; "blunted roots" in hypoparathyroidism.

Examination of the Genito-Urinary Tract. A flat plate of the abdomen may show renal calculi in hyperparathyroidism, Cushing's syndrome, and osteoporosis; displacement of the kidney with adrenal tumor or hyperplasia; decreased density of the bony pelvis in osteoporosis; increased density with metastases from carcinoma of the prostate. An intravenous pyelogram will reveal displacement of the kidney by adrenal tumor or hyperplasia. Displacement of the kidney and adrenal enlargement may also be demonstrated with the aid of perirenal air injection.

Roentgen examination of the chest and of the esophagus after barium may disclose a mediastinal thyroid or parathyroid tumor

A bibliography of fifty-two references covering various phases of endocrinology is appended.

FOREIGN BODIES

Modern Achievements of Roentgenology in the Problem of Residual Projectiles, with Special Reference to the "Boloscope." G. J. van der Plaats. Acta radiol. **23:** 511–532, Oct. 31, 1942. (In German.)

Van der Plaats discusses the different roentgenological methods used for the detection and localization of projectiles (bullets, bomb and shell splinters, etc.) within the human body. The procedures are divided into those before operation (fluoroscopy, aimed radiography, stereoscopy) and those applicable during operation (fluoroscopy, radiography, "boloscopy"). The advantages and disadvantages of all these methods, from the point of view of both radiologist and surgeon, are treated in detail and illustrated by roentgenograms and case histories.

A considerable portion of the article deals with a new localizing instrument developed by the Philips-Metallix Co. of Einthoven and sold under the trade name of "Boloskop" (boloscope). The procedure utilizes two light beams at different angles analogous and simultaneous with two x-ray beams, directed toward the radiopaque foreign body. The lateral and vertical adjustments, requiring but a few seconds, are done by means of fluoroscopy and controlled by a small "cryptoscope." From the position of the light beam, its distance from the body surface, and relation to the operative wound, the location and depth of the foreign body can be directly ascertained. The light beam guides the hand of the surgeon, while the necessary manipulation and eventual readjustments of the boloscope during the operation are left entirely to the roentgenologic personnel. The danger of x-ray burns is minimized in competent hands.

A detailed description of the apparatus is lacking; the reader is, in this respect, referred to previous publications. Since all the references are to the European medical literature, it may be well to mention some of these articles which, in addition to pamphlets of the Philips-Metallix Co., should be easily available in this country: Fesenmeyer, F.: Zentralbl. f. Chir. **68:** 782, 1941; Oberdalhoff: München. med. Wchnschr. **88:** 353, 1941; van der Plaats, G. J.: Fortschr. a. d. Geb. d. Röntgenstrahlen **63:** 167, 1941; Schlaaff, I.: Zentralbl. f. Chir. **67:** 1924, 1940. ERNST A. SCHMIDT, M.D.

RADIOTHERAPY

NEOPLASMS

Tragedy of Malignant Melanoma. Margaret C. Tod. Lancet **2:** 532–534, Oct. 21, 1944.

Miss Tod discusses 100 cases of melanoma from the records of the Holt Radium Institute, Manchester, England, of which she is Assistant Director. She explains that the material is not sufficient for statistical study; nevertheless, the report is of interest inasmuch as out of 100 patients, 50 are still alive, and 8 have been cured for over five years. Seventy-three per cent of those treated early and by radical surgery were alive over various periods of time, an excellent result.

From her experience on this material the author believes that removal, for cosmetic reasons only, of pigmented moles which have long been present but are not growing is inadvisable, unless the victim is willing to undergo radical surgical treatment. Halfway measures have been amply demonstrated to be not only useless but highly dangerous to the life of the unfortunate person who allows an incompetent to treat an apparently benign lesion. If the patient has a pigmented nodule which has begun to grow, radical surgery should be done immediately. Most of these pigmented tumors are highly resistant to radiation, though as a last resort, if the patient is inoperable, radiotherapy may be tried. If regional nodes are invaded, the only possible benefit is from wide removal of the primary growth and the nodes. In such instances, a few cures may be expected. If metastases are widely distributed, no cure by any treatment is probable, but some palliation has on occasion been obtained by heavy irradiation.

Some criticism is made, in the paper, of the general practitioner who treats moles by various home remedies, coagulation, caustics, etc. To anyone who has experience of the worthlessness of such methods this criticism is mild and entirely justified. It called forth, however, several letters (printed in subsequent issues of the *Lancet*) in which Miss Tod is criticized for "betraying" the profession. But how about betraying the patients for whose care one is legally and morally responsible? There is also in these letters some criticism of a few photographs which illustrate late extensions, but these are quite innocuous for a medical journal. Only one letter, that of Hodson (Lancet **2:** 769, Dec. 9, 1944), praises Miss Tod's article as it deserves. As a matter of fact, the criticisms made in the others are mostly beside the point, as anyone who sees a large number of these patients improperly treated knows only too well. FRANCIS CARTER WOOD, M.D.

Cancer of the Tongue: Its Diagnosis and Treatment. Louis H. Jorstad and D. J. Verda. Surg. Clin. N. A. **24:** 1077–1088, October 1944.

A comparison of a series of patients at the Barnard Free Skin and Cancer Hospital, St. Louis, with a private group emphasizes the importance of an early diagnosis of cancer of the tongue. Not only is the prognosis more hopeful if the lesion is controlled in the early stages of its growth, but metastasis is less likely to occur in the secondary (metastatic) zone of lymphatics. In the private series, with a greater percentage of early cases, 70 per cent of the patients showed no evidence of metastasis five to ten years following treatment of the local lesion; in the Barnard group, the corresponding figure was 45 per cent.

An early lingual cancer is one of a few weeks' duration, not over 2 cm. in its greatest dimension, and with no lymph nodes palpable in the drainage zone. The appearance of the primary lesion is usually that of an ulcer with an irregular border. The edges and base of the lesion are woody and hard in consistency. Necrosis, usually absent in the small lesion, becomes a more prominent feature as the neoplasm increases in size. The histologic grade of malignancy is of significance in estimating the prognosis and in certain cases is of value in planning treatment. Cancer of the tongue must be differentiated from syphilis and tuberculosis. A diagnosis of syphilis cannot be based solely upon a positive serological test; a careful history, observation of the lesion under antisyphilitic therapy, and biopsy are essential. Four per cent of the patients in the private series and 12 per cent of those in the Barnard group, with cancer of the tongue, had syphilis also.

Surgery has proved disappointing in eradicating carcinoma of the tongue. Removal of half or all of the tongue produces a "social outcast," as it is extremely difficult for the patient to speak with any degree of clarity after these procedures. Furthermore, the postoperative mortality is prohibitive, particularly in view of the likelihood of recurrence in those who survive operation. The high death rate following the combined operation of resection of half of the tongue plus deep neck dissection contrasts unfavorably with that attending radon implantation into the tongue plus deep neck dissection. In the authors' experience, radium emanation in the form of the "gold seed" or "gold radon implant" has been found more satisfactory in treatment of cancer of the tongue than radium and removable radium needles, and the 1.5-millicurie seed superior to the 1-millicurie glass or gold radon seed. The seeds are implanted, under general anesthesia, 1 cm. apart, around and into the lesion if necessary. Sixty-four per cent of the Barnard series and 90 per cent of the private series showed no evidence of local recurrence or incomplete regression of the cancer following radon implantation.

Local reaction from the radon begins within forty-eight to seventy-two hours and reaches its maximum within two to four weeks. During this period there is considerable discomfort due to swelling and salivation. At the end of two months, a soft, pliable, smooth area should have resulted. In some cases, particularly if the lesion is large and involves the floor of the mouth, it will require one or two months more for the central area of necrosis to separate and fill in with granulation and scar tissue. Persistent induration, particularly if distributed irregularly, is indicative of recurrence.

Surgical resection of the lymph-bearing tissue in the secondary drainage zone (neck dissection) is the treatment of choice in controlling metastasis. In cases with inoperable cervical metastases, distant metastases, or a primary lesion involving contiguous structures, cautery or diathermic removal of necrotic masses or dead bone, alcohol injection or surgical section of nerve trunks, section of sensory roots, interstitial and roentgen irradiation within tissue tolerance are of palliative value, alone or in combination.

Primary Carcinoma of the Trachea. Treatment with Intratracheal Radium; Radioactive Iodine Fails to Show Thyroid Origin. Philip H. Pierson. J. A. M. A. **126:** 206–209, Sept. 23, 1944.

In a 61-year-old male with a three-year history of periodic attacks of cough and sputum (frequently bloody), progressing to wheezing, dyspnea, hemoptysis and reduction of the voice to a whisper, bronchoscopy revealed a tumor involving the anterior tracheal wall above the carina. Biopsies were interpreted as showing low-grade, well differentiated primary adenocarcinoma of the trachea. Tumor tissue removed two days after the ingestion of radioactive iodine exhibited no radioactivity, ruling out the presence of normal thyroid tissue but not necessarily excluding carcinoma of the thyroid. Endoscopic removal of tumor tissue was carried out in multiple sessions followed by radium irradiation by means of an ingenious, specially devised intratracheal applicator. Examination two years after treatment showed the patient to be in good health without evidence of recurrence. A review of the literature by the author emphasizes the infrequent occurrence of the lesion and discloses that resection of a portion of the tracheal wall has been done with varying success, and that intratracheal operations as well as radiation methods employed in the past have generally given poor results.

ISADORE LAMPE, M.D.
(University of Michigan)

Radiation Therapy of Carcinoma of the Breast. M. V. Peters. Canad. M. A. J. **51:** 335–343, October 1944.

The author presents a review of the more striking features of irradiation of mammary cancer. Three main groups present themselves for treatment (Steinthal's classification).

In Stage I the growth is limited entirely to the breast, with no fixation. These cases are further subdivided into (*a*) those with a low index of malignancy and (*b*) very early lesions in which differential diagnosis is impossible clinically. Fifty to 75 per cent of this group will be cured by radical amputation.

Stage II includes cases in which the tumor is fixed to the skin or there is axillary involvement. This group is considered moderately malignant. Twenty to 25 per cent will be cured by radical amputation or will be free from recurrence for five years or more. Postoperative radiation should be well worth while in this group. Of 297 cases reported from the Presbyterian Hospital, New York (Haagensen and Stout), approximately one-half received postoperative prophylactic radiation, with a five-year clinical cure rate of 31.5 per cent, compared with 24.7 per cent for the group not receiving postoperative radiation. Preoperative irradiation is believed to be of even more value, as it may cause partial or total regression of the tumor or the involved nodes, if they are radiosensitive, and render the tumor more defined and freely movable.

Stage III cases are those with more than axillary lymphatic involvement, ulceration, or adherence to the deep tissues. There are three subdivisions: (*a*) carcinoma arising during lactation, (*b*) very malignant types, and (*c*) a less malignant group with extensive spread locally by metastasis. Subgroups *a* and *b* will resist any known form of treatment, even if applied as soon as the lesion is discovered. In this group, the best results are obtained by applying radiation primarily, provided x-ray equipment of sufficient voltage capacity is available under the direction of a competent radiologist. After intensive irradiation of the primary and secondary lesions, a certain percentage of these cases become operable.

For Stage I tumors three series of postoperative irradiation are given, each lasting one week, the first series being started as soon as the incision has healed. The second series is given one month later, and the third three months later. The factors are 200 kv., 0.5 mm. Cu, and 50 cm. distance; 600 r are given to the neck and to the axilla from each of two directions; 1,800 r to the chest wall tangentially in small fractionated doses. Stage II tumors are treated postoperatively in the same way, with additional radiation to the node-bearing regions, 400 kv. being used for two of the three series. The axillary and supraclavicular regions receive 1,800 r over a period of two weeks, and the infraclavicular region is included in one of the axillary fields.

Treatment of Stage III growths, as well as preoperative therapy, must take into consideration the size and extent of the lesion, the degree of lymph node involvement, and the presence or absence of metastasis. The degree of skin reaction is used as a guide. This reaches its peak about two weeks after the treatments are completed. The primary lesion is treated with 400 kv., with a portal large enough to include the whole breast but with the primary beam on the tumor itself. Rays are applied in four directions, superior, inferior, mesial, and lateral, cross-firing the breast tissues. The reduction in the size of the mass is carefully observed and a minimal total of radiation is administered to insure complete restoration of tissue substance for the benefit of the surgeon (where operation is contemplated) and still produce the optimum effect upon the tumor. On completion of treatment, the axillary areas are irradiated to reaction but not to the same degree as the primary lesion, unless the nodes are involved. The whole course usually requires six weeks. If mastectomy is indicated, it may be performed as soon as the reaction has completely subsided.

In recurrent carcinoma and cases with distant metastases treatment varies, but the main objective is to relieve unpleasant symptoms and prolong life. Pain is due in a large percentage of cases to skeletal deposits. Many cases respond well to treatment of the bone lesions, especially if they are the first and sole form of recurrence. Recalcification takes place and life is prolonged one to three years before additional metastases appear.

The data presented as to relationships between age and rate of growth, extent of disease, and three-year survival in cases irradiated preoperatively show that the prognosis in many of the earlier cases of carcinoma of the breast could be improved by preoperative radiation in preference to or in conjunction with postoperative radiation. The statistics further show that the prognosis or expected five-year cure rate is approximately 19 per cent better if considerable postoperative radiation is included in the treatment. The survival rate drops gradually from one to five years in Stage I but sharply in Stage II group around the three-year mark. As a rule, the higher the age group, the better the prognosis, with a difference of only 6 per cent between the two extremes of age. From the tables shown, the following conclusions are reached: (1) Radiation offers the only hope of relief of distressing symptoms in hopeless cases of carcinoma. (2) The most promising group of cases, Stage I, is no doubt benefited by prophylactic radiation, the survey showing the five-year clinical cure rate to be raised from the average of 65 to 75 per cent. (3) In the large group of cases between the two extremes, in which the clinical factors add up to a high degree of malignancy, statistics show that postoperative radiation has raised the survival rate 15 to 20 per cent.

H. T. GUARE, M.D.

Cancer of the Cervix Uteri, 1930–1942. Herbert H. Schlink and Clement L. Chapman. M. J. Australia **2:** 377–379, Oct. 7, 1944.

This report deals with the results of treatment of cancer of the cervix at the Royal Prince Alfred Hospital (Sydney, Australia) from 1930 to 1942. As the result of an agreement made for experimental purposes, the patients were treated by "one full dose of radium, 5,000 to 7,000 milligramme-hours, with one millimetre of platinum screenage to the uterus and two millimetres of platinum screenage to the vagina." After five weeks a radical hysterectomy was done in those considered operable. After five years, the 258 patients studied showed a survival rate of 29.4 per cent and a cure rate of 28.6 per cent, this group consisting of all those "seen with a view to treatment." This rate is compared with a cure rate of 24.2 per cent of 9,051 patients analyzed by Bourne and Williams, reported from 16 centers reporting to the League of Nations registry. The conclusion is drawn that the form of treatment reported saves 4.4 per cent more patients than radiotherapy alone.

In 20 per cent of the 112 patients operated upon, the lymph nodes were found invaded, and the authors state that "the majority of radiotherapists admit that treatment by radium or x-rays has no effect on cancer of the lymphatic glands." In a later communication (in reply to Ham, *vide infra*) the authors give the five-year survival rate for the group with lymph node metastases as 29 per cent and the cure rate as 25 per cent.

When the survivals were broken down by the stage of the disease, the following figures were obtained:

	Cases	Operated	Five-year Survivals
Stage I	17	16	82%
Stage II	62	53	56%
Stage III	129	43	19%
Stage IV	50	None	None

Some interesting figures on the ten-year survivals are also cited.

In a letter to the Editor, commenting on this report, Harold J. Ham (M. J. Australia **2:** 441–442, Oct. 21, 1944) points out that, far from justifying the conclusion reached, the survival rate reported has been surpassed in certain well authenticated reports, especially that of Regaud, who reported 33 per cent five-year survivals; it is therefore hardly proper to conclude that the meth-

ods advocated will save "an additional 4.4 per cent." With a statement that absolute statistics are essential to evaluate results of treatment Ham agrees, but points out that the statistics given are not absolute in that all the patients admitted to the hospital with the diagnosis of cervical cancer are not included. In their finding that cancer cells still persisted in operated cervices, the authors failed properly to evaluate the time element, since regression may extend over two to three months. Since the biological dose is not defined in tissue roentgens, Ham thinks that it is not sufficiently precise for proper research. With the statement that "the majority of radiotherapists admit. . .," etc., cited above, Ham disagrees, since it is at variance with the facts of the response. The authors have abandoned the use of x-ray, yet admit having only a limited experience with it—completely ignoring the great mass of evidence on the subject. Finally, in the analysis of cases in the first three stages, the relative proportions treated by operation and radium and by radium alone are ignored, biasing the result. Ham concludes with a plea for "fair-minded statistical assessment of all known methods of treatment."

[ABSTRACTORS NOTE: The statistical analysis of Schlink and Chapman is indeed pitiful, as Ham points out. No attempt to compare the cure rates of the individual stages with the League of Nations material is made, although the source material in Heyman's reports gives this information in full. In fact, the authors could profit by a study of Heyman's methods of presenting the results of the reporting centers in the Annual Summaries. Furthermore, even assuming that proper sampling methods had been used, comparable with those of the League centers (Ham points out that this is not so), the difference could easily have arisen through the chances of sampling, since the odds against such an event are only about 6 1/2 to 1. Finally, it is a grave question whether the method of radium therapy used was optimum, and the technical details concerning it are very meager.] LEWIS G. JACOBS, M.D.

Diagnosis and Treatment of Cervical Cancer. Frederick V. Emmert and Harold M. Clarke. Surg. Clin. North America **24:** 1185–1197, October 1944.

In a fifteen-year period, 1,000 cases of cancer of the cervix (80 per cent of all admissions to the gynecological service) were seen at the Barnard Free Skin and Cancer Hospital, St. Louis. Six per cent of the patients were between the ages of 20 and 30, 20 per cent between 30 and 40, 31 per cent between 40 and 50, 28 per cent between 50 and 60, 11 per cent between 60 and 70, and 3 per cent over the age of 70 years. Fifteen per cent of the women were nulliparous. In only 2 cases did the cervical carcinoma occur during pregnancy.

Every woman admitted to the gynecological service is examined with a vaginal speculum, and a biopsy specimen is taken of all suspicious erosions of the cervix. This procedure is preferred to cautery conization of the cervix, as the intense heat may destroy early evidence of malignant change. Cancers are graded in accordance with the League of Nations classification. While the immediate mortality following irradiation is considerably less than that following hysterectomy, the late complications leading to death are definitely more frequent. In Stage I cancers, radical surgery in patients who are good operative risks presents definite advantages over irradiation. In Stage II cancers, radical surgery gives too high a primary mortality, hence irradiation of the primary lesion is advisable. It is not certain whether irradiation with removal of the individual iliac nodes will increase the survival rate. In Stage III and IV cancers, irradiation is the only means of treatment.

In all cases in which radiation alone is to be used, a calculated dose of 2,500 r to the site of the tumor is administered. The factors are 200 kv., 18 ma., distance 50 cm., with a Thoraeus filter. In small persons, four ports, two anterior and two posterior, usually suffice, while in extremely large women, six ports, including a perineal port, are sometimes necessary. Treatment is given to two ports daily, 250 r to each. When radical surgery is contemplated, only half the amount of roentgen radiation is employed.

If a patient is considered a poor operative risk, further treatment consists of radium implantation. Under twilight analgesia, the uterus is sounded and the cervical os dilated so that it will accommodate a brass capsule containing, in tandem, three 25-mg. needles in 0.5 mm. of platinum. In the ordinary case two 25-mg. needles in 1 mm. of platinum are imbedded in a piece of sponge rubber (which has been trimmed so that it will fit snugly up against the cervix) in such a manner that one needle will fit into each lateral fornix. An additional 10-mg. needle in 1 mm. of platinum is inserted in the sponge rubber so that it will lie across the area of greatest involvement. The sponge rubber is then placed against the cervix so that the radium is in the desired relation to the surrounding structures. Stout threads are fastened to all radium needles and these threads are tied to a vaginal pack which is inserted over, under, and behind the sponge rubber applicator, increasing the distance of the radium from the bladder, rectum, and vaginal walls, and holding the applicator firmly in place. It is believed that a full dose, between 5,000 and 6,000 mg. hours, well filtered and well distributed, should be given to every patient for whom radium is prescribed.

In surgically treated cases, operation is usually carried out three weeks after the completion of x-ray therapy. Radical abdominal hysterectomy, with removal of the entire uterus, a good portion of the upper vagina, the surrounding connective tissue containing the lymph vessels of the uterus, and at times the regional nodes, is preferred for the early cases of cervical cancer.

Discussion on the Radiotherapy of Malignant Disease of the Ovary. Alan Brews, Margaret C. Tod, and Frank Ellis. Proc. Roy. Soc. Med. **37:** 720–730, October 1944.

This discussion was opened by Brews with a general consideration of malignant ovarian tumors and the reported results of surgical treatment. Miss Tod followed with an outline of the radiotherapeutic technic used in the Holt Radium Institute (Manchester), and Ellis contributed figures from the Sheffield Radium Centre.

At the Holt Radium Institute, radiotherapy is given only when the tumor has been incompletely removed or is inoperable. Prophylactic irradiation following complete surgical removal is not considered of value. Treatment is primarily by x-ray, but radium is regarded as a useful adjunct when the uterus is secondarily involved or when the vaginal vault is invaded after hysterectomy. The tendency in treatment has been toward larger fields and higher dosage. Thus, the old technic of using four 10 × 15-cm. fields about the pelvis has been discarded and a new plan evolved whereby the entire abdominal cavity is irradiated.

The method employed at present in the Holt Insti-

tute was devised three years ago and utilizes a simple device called a "trunk bridge." Treatment is given to three portals, a direct posterior 30-cm. circular field and two oblique 20 × 30-cm. anterior fields. The "bridge," used to determine the anterior ports, consists of a large baseboard on which the patient lies and is centered. At the side is a post holding a marker set at a 30 degree angle, adjustable as to length. Bolus bags are placed between the skin and the marker to ensure full scattering, and the tube, at a 60 cm. F.S.D., is set to the 30 degree marker. Treatment is given to all three fields daily, starting with 40 r per port and increasing until 100 r is reached. A total tumor dose of 3,000 r can usually be given in three or four weeks. Since large areas are treated by this method, not only must the local skin reaction be watched but the systemic reaction of the patient as well. Generally, a fall in lymphocytes to 300 per c.c. is a danger signal even if the white count is a little below normal, as the latter may drop suddenly with continuation of treatment.

An attempt has been made to establish a relationship between the change in the white blood cell count and the total amount of x-ray absorbed, with the aid of Mayneord's simplest formula for calculating the integral dose. Estimating a 10 per cent loss in the scattering material used in packing the "bridge" and an additional 5 per cent for side packing for narrow patients, the average integral dose delivered in twenty-one to twenty-four days is 48 megagram roentgens. Graphs were made plotting the white counts of 34 patients against the integral dose. The count dropped to 2,500 per c.c. in fourteen days after 20 megagram roentgens had been delivered, at which level it remained fairly stationary, until treatment ceased, when it began to rise. The fall in the total white cell count was paralleled by a drop in lymphocytes to 300 c.c. Although the number of patients treated is insufficient to warrant conclusions, the author's observations here and in a series of seminomas of the testis indicate that a 3,000 r tumor dose can be given safely to the abdomen with the above technic. Further investigation is desired to determine if smaller doses over a longer period of time but with a greater total dose are preferable. A shorter treatment period is considered not feasible because of the necessity of using small initial doses.

Miss Tod's statistics are, according to her own statement, not such as to permit conclusions. Of her most recent series of patients, 26 treated in 1941 and 1942, 13 were alive after one to two years, and this she states represents "not merely a survival of women whose disease has been temporarily arrested, but 92 per cent of all those alive are free from symptoms."

The results reported by Ellis from the Sheffield Centre are based on 105 cases of ovarian carcinoma treated from 1932 to 1939. The series included both recurrences after operation and operated cases without recurrence. Of the total number 25 per cent were alive ("when traced"). To assess the value of radiotherapy, only the cases with definite recurrences or residual growth are considered. Of 68 such patients, 44 per cent survived more than a year, while of 20 untreated patients only 25 per cent were alive after a year. The corresponding figures for three-year survival are 22 per cent and 5 per cent.

The prognosis proved to be more favorable in pseudomucinous cysts than in papillary adenocarcinomas and in unilateral than in bilateral tumors. A combination of x-rays and radium appeared to give better results than the use of x-rays alone. The survival period seemed to improve as dosage was increased, but the figures on this point are admittedly not significant statistically. LESTER M. J. FREEDMAN, M.D.

Malignant Lymphomas of the Spinal Epidural Space. D. J. Verda. Surg. Clin. North America. **24:** 1228-1244, October 1944.

Malignant lymphomas may arise in the epidural space itself or may reach that space secondarily, by migration from near-by regional lymph nodes. A case of each type is presented. The symptomatology of malignant spinal epidural lymphomas does not differ essentially from that of other cord tumors; the neurologic findings are similar to those of other epidural tumors.

Dyke divided the roentgen criteria for diagnosis and localization into two classes—in the major class, bone destruction, appearance of the pedicles and evaluation of interpediculate distance, and distortion of the paraspinal tissues; in the minor class, bone proliferation, abnormalities of the intervertebral disks, kyphosis and scoliosis, and calcification. About 80 per cent of the epidural spinal cord tumors are demonstrable by the simpler roentgenographic methods. The most reliable procedure for the localization and investigation of cord tumors is myelography, either with air or lipiodol.

Even though it proves impossible to remove the tumors themselves, laminectomy may relieve the pressure on the cord. In a surgical consideration of spinal epidural lymphomas, the cases should be segregated into two main groups, those in which neurological symptoms are an initial manifestation, prior to any recognizable lymphadenopathy, and those in which spinal cord compression is a terminal manifestation. In the first group, laminectomy should be performed as soon as the level of the tumor can be accurately established. In the second group, surgery is not indicated until roentgen therapy has been given a thorough trial.

One week following laminectomy, in the patients with primary neurologic symptoms, roentgen irradiation to the region of the vertebra where the tumor was located is begun. Preferably, right and left oblique ports are used, directly over the operative site, with the following factors: 200 kv.p., 18 ma., 50 cm. F.S.D., filtration 0.5 mm. Cu, intensity 85 r (with back-scatter 20 × 20 cm.) per minute, the port size depending upon the size of the tumor and area to be treated and the degree of epidural involvement. The daily dosage is 100 r to alternate ports until a total tumor dose of 900 or 1,000 r is reached. In some cases subsequent courses of roentgen therapy are necessary. In the patients with lymphomatous involvement prior to neurologic symptoms, roentgen irradiation is routinely administered to the primarily involved regions. The technic for irradiation of the vertebral area is similar to that above except that, as a rule, larger parts are covered to irradiate all of the affected mediastinal or lumbar nodes. If a plaster body cast is necessary because of vertebral destruction with malalignment of the spinal column, a posterior window may be cut over the area to be irradiated.

Adequate X-Ray and Radium Dosage. Edwin C. Ernst. Surg. Clin. North America **24:** 1003–1021, October 1944.

It has not been fully appreciated or realized that roentgen and radium rays possess powers of producing, directly or indirectly, varying degrees of physical, chemical, and biological change. The same type of

cancer may react differently to the same form of radiation in various persons. Again, roentgen or radium rays may inhibit or destroy in a dual capacity the living tissues, depending upon the timing and manner of irradiation. The reactions which tissues show to irradiation and the degree of cell sensitivity to like roentgen dosage may also differ. Similarly, the latent periods of different cell structures vary with different tissues. In some the "time" interval between irradiation and the resulting physical reaction is relatively short, while in others it is more prolonged, even though the type, quantity, and method of administering the radiations are identical. Usually, large amounts of radiation applied in a short time prove less effective than smaller divided doses of equal intensity applied over a longer period.

The successful treatment of cancer is not solely dependent upon elaborate surgical, roentgen, or radium equipment, but equally upon clinical experience, radiation judgment, and the cooperation of physicians in the various fields of medicine.

The author discusses specifically cancer of the breast, cancer of the skin, cancer of the larynx, pharynx, and tonsils, and cancer of the cervix. Cervical cancer demands a greater number of complex combinations of x-ray and radium technics than any other single cancer. Its effective treatment is largely dependent upon the homogeneous distribution, proper timing, and coordination of the roentgen and radium treatments. The importance of recording essential physical and technical radiation factors is emphasized. The treatment record should include not only the air or surface dose in roentgens, the quality of the rays, half-value layer, and daily and total dose delivered to each portal, but also, more particularly in the case of abdominal neoplasms, the size of the patient, since this indirectly predetermines the amount of effective radiation reaching the tumor.

NON-NEOPLASTIC DISEASES

Discussion on Radiotherapy in Chronic Inflammatory Conditions with Special Reference to Mycotic Infections. Alexander B. MacGregor, John Blewett, I. G. Williams, and Finzi. Proc. Roy. Soc. Med. **37:** 717–719, October 1944.

MacGregor's part in this discussion, which is published in abridged form, is concerned solely with actinomycosis. He is said to have advocated a combination of radiotherapy, surgery, and chemotherapy, but no details are given.

Blewett found roentgen therapy of value in superficial infections of the skin and subcutaneous tissues (as furunculosis), osteomyelitis, chronic mastitis, tuberculous adenitis, some cases of chronic arthritis, and early ankylosing spondylitis, as well as in mycotic infections. Of these last, he had a series of 58 cases, of which 55 were proved actinomycosis, 1 blastomycosis, and 2 unproved. Of the 55 proved cases of actinomycosis, 39 were of the cervicofacial and 16 of the abdominal type. The period of observation ranged from six months to ten years. Of 29 patients with cervicofacial actinomycosis receiving radiation therapy, often following failure of other methods, 25 were free of disease; there was a single relapse requiring subsequent surgery, and in the 3 remaining cases no follow-up was obtained. Of 10 patients receiving no x-ray therapy, 6 were known to be free from the disease and no records were obtainable for the other 4. Poorer results were obtained in the 16 cases of abdominal actinomycosis. Of 9 patients treated without x-ray, 5 remained free of disease, 1 was improved, 2 died, and in 1 no follow-up was obtainable. Of 7 patients treated by x-rays, 1 was free of the disease, 4 had died, 1 was still under treatment, and 1 was untraced.

A dose of 300 r was repeated at three-week intervals until all induration disappeared. More intensive treatment induced skin damage and abscess formation. The average required three months.

Williams reported that potassium iodide was still believed to be of value in the treatment of actinomycosis at the Middlesex Hospital. Radiotherapy, however, he designated as "the most useful single therapeutic measure available today," roentgen irradiation being considered simpler and more efficacious than radium. The best results were obtained using a hard ray, 1.3 mm. Cu h.v.l., and fractionated dosage. Daily doses of 100 to 150 r (w.b.s.) were given for a total of about 2,500 r over fields sufficient to cover the entire area involved.

Of 43 patients, 26 had cervicofacial involvement, 12 had the disease in the right iliac fossa, 2 had pleuropulmonary lesions, and in the remainder other sites were involved. The ages ranged from twelve years to sixty-five years and in only 14 per cent was there a history of association with animals or agriculture. There were 6 deaths; none of these was in the cervicofacial group.

Finzi closed the discussion, stating a preference for small doses of radiation for both actinomycosis and tuberculosis, 50 to 60 r, as better results are obtained without danger of skin changes. For actinomycosis he believes that radium gives better results than x-rays "if one can get an adequate dose to the deepest part of the disease without giving the skin a big dose."

LESTER M. J. FREEDMAN, M.D.

Radiation Treatment of Ganglia of the Wrist. Robert J. Reeves. South M. J. **37:** 584–586, October 1944.

Fifteen cases of ganglia of the wrist were treated by roentgen irradiation by the author and followed for more than one year. In 87 per cent of these cases, the lesion cleared up with no skin damage or deformity. The method of treatment was as follows: The ganglion, if more than 1 cm. in diameter, was aspirated and then given 400 or 500 r at 200 kv. with 0.5 mm. Cu filter, half-value layer 1.1 mm. Cu. If the tumor persisted, monthly treatments were given, with three treatments as the average. The action of the x-rays is one of counterirritation with resulting fibrosis and destruction of the endothelial secreting cells. The cosmetic results are better with roentgen therapy than with surgery and no hospitalization is required.

RADIATION EFFECTS

Irradiation Pneumonitis. Report of a Case. Theodore O. Alexander. Bull. Johns Hopkins Hosp. **75:** 199–208, October 1944.

A case of Hodgkin's disease receiving roentgen therapy is described. It is of interest because of the development of severe respiratory symptoms shortly after a course of irradiation to the mediastinum, where the adjacent lung tissues necessarily were not shielded. Roentgenograms showed an extensive pneumonitis. In the nine months from the beginning of therapy to the time these changes appeared in his lungs, the patient

had received a total of 6,776 r to the mediastinum. At autopsy, the lungs showed lesions similar to those which have been produced experimentally by over-irradiation. A patchy exudate composed of edema fluid, a few red and white cells, fibrin, and fibrinous-hyaline membrane was found involving the greater portion of each lung. There was widespread organization of this exudate. A few microscopic foci of Hodgkin's tissues were found in the bronchial lymph nodes and in the pericardium. There was no Hodgkin's tissue in the lungs.

Hematologic Complications of Therapy with Radioactive Phosphorus. Louis H. Hempelmann, Jr., Edward H. Reinhard, Carl V. Moore, Olga S. Bierbaum, and Sherwood Moore. J. Lab. & Clin. Med. **29:** 1020–1041, October 1944.

The authors' observations are based on 100 patients treated with radioactive phosphorus at the Washington University School of Medicine, and followed for a sufficient period of time to permit evaluation of results. They believe that this form of therapy induces excellent remissions in patients with polycythemia vera, chronic myelogenous leukemia, and chronic lymphatic leukemia. In this series of cases an attempt was made to bring the blood count of the patients with leukemia to normal levels, rather than to treat symptomatically, as most investigators prefer.

In 44 of the 100 patients, a thrombocytopenia of less than 100,000 per cubic millimeter developed (in 33 of these the platelet count was less than 50,000); 41 showed a leukopenia of less than 3,000; and in 36 the red blood cells fell by more than 1 million to a level of under 3.5 million. The authors warn that these hematologic complications may be delayed weeks or months after the last dose of radioactive phosphorus has been given, and because of the variation in susceptibility to the effects of this form of radiation therapy, dosage regulation must be individualized to a high degree.

ELLWOOD W. GODFREY, M.D.

X-Ray Exposure in Manufacture and Operation of Certain Electronic Tubes. A. F. Bush, H. T. Castberg, and D. G. Macpherson. Public Health Rep. **59:** 1045–1047, Aug. 11, 1944.

The authors call attention to a possible hazard in the manufacture and operation of high-vacuum electronic tubes. In their investigation they found that during the manufacture, testing, and operation of such tubes, measurable amounts of potentially harmful x-rays were produced. The tubes were tested or operated at voltages above 25 kv. The presence of x-rays was detected with fluoroscopic screens and measured by means of the Victoreen minometer and dental x-ray films. In one industrial situation studied extensively, the exposure of operators was found to be as high as 2.5 r per day (provisional tolerance dose 0.1 r per day, according to National Bureau of Standards). Once this hazard was recognized, it was possible to reduce the intensities below the provisional tolerance dose by the use of sheet lead, sheet steel, and lead glass.

Effects of Repeated Irradiation of the Gastric Region with Small Doses of Roentgen Rays upon the Stomach and Blood of Dogs. W. C. Hueper and J. de Carvajal-Forero. Am. J. Roentgenol. **52:** 529–534, November 1944.

This study was undertaken to determine the possible action of roentgen therapy upon the erythropoietic activity of the bone marrow and upon the blood through a possible effect upon the production of the so-called "intrinsic factor" of Castle. It was found that roentgen rays given in doses of 15 to 120 r up to a total of 4,875 r within twenty-five weeks over the gastric region of dogs caused only minor anatomic changes in the gastric mucosa and a transitory and moderate anemia of the secondary type, followed by an erythrocytotic phase after the cessation of the actinic treatment. Roentgen rays administered in doses of 300 r, up to a total of 6,000 r within four weeks, produced a considerable loss in body weight, a moderate to severe secondary anemia, and perforating gastric ulcers at the end of this period. In neither instance was there evidence of anemia of the pernicious variety, which would have resulted if the treatment given had interfered with the production of the "intrinsic factor" generated by the gastric mucosa, according to Castle. The chief cells of the gastric mucosa are, according to the observations made, definitely more sensitive to the action of the roentgen rays than any other cellular element of the gastric mucosa.

The histologic changes found in the organs of the dogs which were treated with larger doses over a shorter period of time are described in detail.

CLARENCE E. WEAVER, M.D.

Radium Metabolism in Rats, and the Production of Osteogenic Sarcoma by Experimental Radium Poisoning. Robley D. Evans, Robert S. Harris, and J. W. M. Bunker. Am. J. Roentgenol. **52:** 353–373, October 1944.

The effect of radium given orally and intradermally to rats is the subject of this report. The oral administration of 25 to 100 micrograms of radium resulted about a year later in a high incidence of primary osteogenic sarcoma, usually in the vertebrae, with metastases to the lungs and other organs. The animals exhibited many of the classical symptoms of radium poisoning as seen in human beings. The bones showed hypercalcification at the ends. They were fragile, but fracture healed satisfactorily. At death an average of 3 per cent of the radium administered orally remained in the body, while 50 per cent of that injected intradermally was retained. Studies of the various tissues for radium content showed that the bones had at least 100 times the radium concentration of the richest soft tissue (lung). It was found that the rat could not be used for obtaining an estimate of the toxic dose of radium in man. To produce chronic symptoms similar to those in man, the rat requires some 150 times as much radium per kilogram of body weight and some 250 times the skeletal ratio of radium to calcium. L. W. PAUL, M.D.